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THE TRIUMPHS OF PALLIATION IN RADIATION THERAPY*

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THIS Fiftieth Anniversary Meeting of the American Roentgen Ray Society is a momentous occasion. It is another great milestone in radiology with its very atmosphere radiating honor and glory, progress and achievement, success and triumph which the labors of radiology so richly deserve.

It is a fitting time to pause and reflect on the records of our achievements. These are many and marvelous, and it would indeed be difficult and embarrassing to discriminate against these accomplishments with respect to either diagnosis or therapy.

I am happy to have this privilege and opportunity to discuss with you one of the great problems in cancer therapy that has always been close to me with respect to the value of roentgen and radium treatment in advanced cancer. Some of the results may only be transient and of a short-lived character, but it is this idea and objective of a palliative effect of irradiation that must be brought back to the spotlight of our therapy program, and re-emphasized as one of the outstanding benefits to be obtained by irradiation, even though the records of good results cannot be shown in terms of statistics.

An intimate association with this advanced, recurrent, so-called hopeless type of cancer patient has obsessed me with the firm conviction that if radium and roentgen rays were to be acknowledged as of no actual value beyond ordinary palliative benefits, then these agents of irradiation for advanced cancer should be considered as having achieved and earned their rightful high place in the therapeutic armamentarium of medical progress and science.

There are few radiologists who will not regard some of the most outstanding results of irradiation in their experience as benefits of a palliative character.

But, as the total number of early cases of cancer of all anatomic sites for both surgical and irradiation management is approximately less than 35 to 40 per cent, it is very evident that the remaining great majority of advanced cases must receive some help as against the alternative of

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doing nothing. There are comparable, dire circumstances in other departments of medicine.

It is distressing to observe the futility of any kind of treatment for many of the advanced cardiorenal, arthritic, metabolic, tuberculous, neuropsychiatric, as well as a host of other pathologic entities. This hopeless situation is accepted by many physicians as well as patients with complacence and even optimism. Irradiation, on the other hand, can maintain an individual, with hopeless cancer, comfortable and ambulatory for indefinite periods of time—as much as several years or more.

Palliative benefits of irradiation are determined, not by tables and statistics, not by estimates of increased longevity cycles, but an improvement in health and strength, gain in weight, relief of pain and discomfort, regression and complete healing of ulcerations which may be large, ugly, fungating and odoriferous, by lessening or completely controlling hemorrhage, by the healing of metastatic bone lesions and repair of certain pathologic fractures, by the suppression of cough and dyspnea in lung and mediastinal metastasis, by the retardation of localized and generalized metastasis, and very often by the prolongation of life, as well as many other well known and universally acknowledged benefits to be obtained by irradiation.

Supportive medical measures and neurosurgical methods are always an important and, at some time in the course of the disease, a necessary adjunct. Even though life is not prolonged in many instances, the improved well-being and the relief of pain are a satisfaction and comfort which cannot be equaled in the management of many other hopeless diseases.

Relief of pain is often a very dramatic effect of irradiation, particularly in carcinoma of the cervix—Stage IV—or so-called frozen pelvis extent of involvement; in carcinoma of the breast when pain may be related to axillary or supraclavicular lymph node infiltration, or to relief of pain and dyspnea due to metastatic mediastinal lymph node adenopathy, but predominantly to relieve pain as a result of skeletal metastasis secondary to breast carcinoma.

The healing effect of irradiation for inoperable, ulcerating, odoriferous carcinomas of the breast and also other types of soft tissue tumors is a very remarkable benefit.

Control of bleeding in carcinoma of the cervix is a common beneficial result. This may be achieved in inoperable carcinoma of the bladder and rectum. This is generally a very gratifying result and can often be an emergency benefit.

Abdominal carcinomatosis of ovarian origin may be radiosensitive and is always worth while considering. The palliative effects may be very dramatic.

Brain tumors, either inoperable or recurrent, may be benefited to an unusual and remarkable degree, contrary to the disparaging reports of bad results because of the well known resistance of these tumors to irradiation, as has been detailed in the voluminous reports of the literature in the past. Better results are now seen because of a greater enthusiastic approach to the planning of the treatment.

More than 50 per cent of the bronchogenic carcinomas are inoperable at the time of diagnosis, but these patients may be made comfortable from the standpoint of mitigating pain, dyspnea, and hemorrhage. While 50 per cent of these cases may be considered to be explorable at the time of diagnosis, less than half are found to be resectable. The so-called Pancoast or sulcus tumor is inoperable but may be relieved of the excruciating pain by intensive irradiation even though morphine medication is generally of little value.

Irradiation of recurrent tumors and lymph node metastasis from carcinoma of various anatomic sites may result in beneficial effects that are outstanding.

The lymphoblastomas and leukemias still remain conditions for which roentgen therapy is generally regarded as the first treatment of choice.

Advanced inoperable cancers of the

larynx, pharynx and intraoral cancers are common conditions that may be benefited.

Inoperable superficial and local recurrent lesions are also conditions in which intensive irradiation should be instituted.

Preoperative irradiation to supplement palliative surgery for advanced carcinoma of the breast, soft tissue tumors, bone tumors, hypernephroma, and a host of other conditions results in beneficial effects that experienced radiologists see but do not write about. A complete record of achievement cannot be stated by mere words or case reports.

Irradiation of the ovaries in cancer of the breast that has recurred after radical surgery in younger individuals who are still menstruating may result in a very phenomenal and sensational benefit. The results, however, are variable; they are not consistent and the beneficial effects are usually of fairly short duration.

Steroid hormone therapy in recurrent and metastatic cancer of the breast may show a remarkable degree of subjective benefit as well as objective changes in the roentgenograms. We have limited the use of estrogens to soft tissue metastases in individuals over sixty years of age, while androgens have been confined to patients with bone metastases.

In my experience, roentgen therapy has been more satisfactory than hormone therapy. Relief of pain, regression of local recurrences, soft tissue metastasis, as well as bone regeneration and metastasis of the spine, pelvis and extremities are effects that have been more consistent and striking with roentgen rather than with hormone therapy. A combination of irradiation and hormone therapy is sometimes worth while.

Technical procedures for palliative irradiation must be carefully planned. A routine so-called mathematical procedure cannot be followed. The treatment must be individualized. The patient with inoperable cancer must never be the object of careless or indifferent treatment. It requires a special and greater effort, as well as a keener interest and enthusiasm than is generally manifested in the routine management of this hopeless disease and individual.

Each patient is a problem according to age, physical condition, and extent of involvement. Marked differences in radiation treatment for tumors of identical anatomic sites will occur.

Other factors that govern results of irradiation are the daily rate and intensity, size of portals, the bed of the tumor, complicating infection, the host, endocrine conditions and metabolic disturbances.

Manifestations of sensitivity and resistance are so variable that clinical results of treatment are the final determining factors on this score.

The designation of a possible, radiosensitive or radioresistant tumor by histopathologic evaluation is no criterion as to curability. Sections of different areas of the same tumor may show all of the features of various cellular differentiations. A radiosensitive lymphoblastoma is rarely curable but a resistant cancer of the skin and lip is usually curable by irradiation.

Our changing concepts regarding the skin dose are important considerations. The best technique is that which will deliver an effective lethal dose to the involved area and still preserve the integrity of the normal surrounding structures. It is now generally conceded that there is no specific benefit from any particular quality of radiation. The biologic effect of irradiation, whether the primary source is that of 1,000 kv. or of 100 kv. is of no practical or immediate importance. The quantitative difference may be adjusted by a cross-fire technique that will administer a depth dose of sufficient intensity to destroy tumor tissue.

The equipment that is available in practically every institution with ranges of 200 kv. can be considered suitable not only for the treatment of cancers that are ordinarily curable by irradiation but also for routine palliative measures.

Supervoltage therapy may have some advantages in certain inaccessible cancers or so-called "deep-seated" tumors. Much work has to be done to prove this superiority in the final clinical results. Irradiation with betatrons and synchrotons is still of incompletely proved value. The revival of the so-called "grid" technique and the recent experiences with a "rotary tube" in irradiation procedures seems to show some advantage in effecting greater depth dose values. Further research along these lines is necessary but the outlook is promising and should be of tremendous value because of its application in voltage ranges of about 200 kilovolts.

Radiations from unstable isotopes are invaluable in research but of very limited value in cancer therapy, as far as experience has shown up to the present time, except in the treatment of cancer of the thyroid.

Should treatment procedures for palliation be strenuous and vigorous; should they be conservative and avoid risking the comfort of the patient and aim to mitigate skin reactions; or should modifications of the predetermined plan of treatment and total dosage be temporized so that the biologic effects and benefits will be slight or impossible simply because the clinical character and extent of involvement are far beyond any reasonable chance of help or benefit as to cure?

Should the aim be confined to relieving pain or should efforts be made only to heal sloughing, or odoriferous ulcerations? These are questions that the experience of the individual radiologist must decide.

The problem of transportation in many instances may be a handicap and hospitalization becomes necessary.

The factors of late radiation ulcers, radiation osteonecrosis, leukopenia and anemia which cannot always be avoided if strenuous treatment is to be carried out, may be distressing complications, but if cancer is to be controlled, these changes will probably not be of great importance.

Radiation sickness is always a disturbing condition, and, while there are no specific remedies, there are many supportive measures which can be carried out to make the discomfort more tolerable and permit the completion of a predetermined plan of treatment.

There arise strange circumstances and situations in the problem of treating a dying individual or one who knows that he has only a short time to live. The physician cannot always regulate the many intangible influences that may render the early cancer incurable and the advanced cancer uncontrollable. He should be equally cautious in guaranteeing a cure or dwelling on the futility of treatment. One of the many delicate and unpleasant situations in medicine is the problem of how and when and to whom the truth about the diagnosis of cancer and the prognosis is to be told. Courage and emotional stability are variable qualities in human beings.

While fear and ignorance conspire to perpetuate a false legend of a stigma of an incurable disease and regard the diagnosis as a verdict of death, nevertheless there are very satisfactory and practical methods of approach to management and treatment that instill confidence, afford consolation and comfort as well as peace of mind and cooperation.

The problem of morale is one that has exhausted all controversies on this matter. The ever-burning question of a "cure worse than the disease" enters into the picture of this problem. The patient is given reassurance with the frequent result that the seriousness of the disease is minimized or a word-picture of an apparent curable condition is portrayed.

The patient notices that much is being done for an apparently trivial condition. The controversy is ever present about the proper answer to the constant queries of the patient: "Is this cancer, and if not, why do I need x-ray treatment or an operation?"

Special problems arise for each case. While the average individual is suspicious of his trouble, he generally does not want

to be told frankly. He has nothing left but hope and this false hope must be encouraged and extended under any circumstances. Friends and relatives are often affected more than the patient by the obvious failing in health and strength, by the weakness and fatigue and also by the wasting and emaciation, which are very distressing situations. They accordingly often demand that the patient be kept in ignorance. It is sometimes necessary and advisable to tell patients who have advanced cancer that they cannot recover. These are circumstances for special consideration.

The roles of the surgeon and radiologist in the treatment of cancer are now fairly well defined. Each speciality holds a recognized place in the treatment of reasonably early cases of cancer for which cure may be expected.

Decisions as to operability must be individualized and modified according to the training, experience, facilities and equipment, but the regulation of the kind of treatment must finally rest on the special ability and skill of the surgeon or radiologist according to the particular anatomic site of cancer under consideration.

Roentgen treatment must never be considered as a substitute for surgery which is still the outstanding proved method of effecting a cure for the so-called "deep-seated" cancers—notably of the brain, lung, gastrointestinal and urinary tract regions.

Irradiation remains the method of choice for the superficial cancers of the skin, lip, intraoral cancer, and cancer of the uterine cervix.

There is a renewed tendency to consider irradiation as a method of choice for cancer of the larynx. The reports of increasingly good results are becoming very voluminous, and most encouraging, and include cases with a wide range of anatomic extent of involvement—virtually consisting of unselected cases.

The final record of results of surgery and irradiation for "early" cases is improving but the numbers have been too small and discouraging to significantly alter the final end results.

The training of residents in radiology offers special opportunities for the study of the cancer problem. These advantages are extraordinary because they involve intimate contacts with the clinical course of cancer, and an acquaintance and broad perspective with results to be achieved with the various methods of treatment.

Modern laboratory equipment and improved methods of application have stimulated a renewed interest in procedures of early diagnosis and treatment. These circumstances have been a great incentive to the young resident; they have been enlarged and strengthened by a dove-tailing enthusiasm and interest throughout the various allied specialties of the hospital staff, resulting in a splendid collaboration and team-work and a mutual effort to examine the details and results of the immediate and practical projects of changing techniques and equipment.

These advantages have also been supported by a vigorous campaign to arouse the interest and support of the family physician, together with a national campaign to educate the public. While these activities have contributed much to improve our knowledge of cancer and to hold this problem a burning question, the great massive surge of inoperability at the time of diagnosis persists and this amazing situation continues to an alarming degree in spite of the improved facilities for early diagnosis and treatment.

Relentless efforts to make an early diagnosis of cancer in a greater number of patients must be continued if greater progress in the management of this disease is to be achieved.

The best interest of the cancer patient must involve the combined efforts and skill of the family physician, the surgeon, and the radiologist. Bronchology, urology, gynecology, pathology, as well as radiology, are special departments of importance for diagnostic accuracy.

Progress in radiation therapy is not retarded or overshadowed by the great advances and successes of surgery. Neither surgery nor irradiation is the final answer to the cancer problem, but thousands of cures and marvelous palliative benefits by surgery and irradiation are monumental records of medical achievements.

It is gratifying to note the interest and progress in the development of improved technical procedures of irradiation, particularly for the treatment of early or estimated curable cancers. Emphasis has very properly been directed to improving and recording results of so-called "cures" in terms of statistics for the early cases.

Records of accomplishments are vital. They are a source of encouragement and an incentive for further improvement.

It would be a precocious kind of scientific vision that would ignore the importance of maintaining accurate, statistical records for the probable curable group. An insatiable curiosity with respect to the possible good results to be achieved by irradiation in the early cases must be constantly and rigidly observed.

The priceless heritage of the radiologist is the opportunity as a physician to maintain a close relationship with individuals afflicted with disease, and especially with cancer. This intimate contact calls into play all the potentialities of the healing art. His responsibilities are a constant reminder of the training and experience which he owes to the suffering individual.

Not only knowledge of the disease, its clinical and pathological characters, but also a special training and skill of the ever-changing physical equipment for treatment and the newer meticulous methods of diagnosis are the weapons that must be used.

The cancer patient must be the object of kindness, tenderness and sympathy, as well as skill and understanding.

While it is true that irradiation has effected marvelous clinical results as well as actual cures, it is likewise true that the expectations of the public and even the medical profession far exceed the real possibilities.

As these triumphs pass in review and the numerous processes of expediency and unprecedented paradoxes continue to reveal disappointing casualties from too much enthusiasm and wishful thinking, still many of these problems of management will also require psychological as well as actual physical assistance.

The radiologist is a scientist but, above all, an artist and he must bring into play all of the manipulations of mental encouragement as well as physical aids that are known to medicine.

The advantages for an outlet of the pent-up natural resources of the physician for psychotherapy are extraordinary.

The progress in radiology, and especially in therapy, has been in tune with the magnificent achievements of medicine. Unfortunately, the incidence of inoperable cancer is still too high and even overwhelming at the time of diagnosis. Even apparently operable cases still show a heavy toll of recurrences. The medical profession and the public look to the radiologist for an expert opinion about methods of diagnosis, management and treatment as well as problems of complications. The management and treatment of cancer still remains predominantly a radiological problem.

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GROWTH AND SPREAD OF CANCER OF THE CERVIX UTERI*

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IN OUR usual concentration on improvement in methods for the early detection of cancer of the cervix uteri, or its more effective treatment, or a more widespread dissemination of knowledge of these methods among the medical profession as a whole, little attention is paid ordinarily to the natural history of the disease, how long it lasts when untreated, where it spreads, or how it kills its hosts. Considerable information has been accumulated in the past on these matters, but much of it has been buried by time in the bound volumes of medical journals or has not been adequately emphasized. It is the purpose of this discussion to bring to notice some of these contributions and place them together in such a way as to give a picture of the whole course of the growth of untreated cervical cancer, as well as to add some corroborative evidence from our own clinics.

Onset of Cancer of the Cervix: Carcinoma in Situ. The first description of carcinoma in situ or preinvasive carcinoma is usually ascribed to Schottländer and Kermauner[9] in a book published in 1912. The widespread recognition of this pathological entity in this country is of only recent development, however, and in fact dates from 1933 or later. It has come into much prominence in the last six years since the publication by Papanicolaou and Traut[7] of their monograph on the "Diagnosis of Uterine Cancer by the Vaginal Smear." It is by the widespread use of the Papanicolaou method that many cases of carcinoma in situ are being detected today, since frequently this condition produces no symptoms, is unsuspected by both patient and physician, and is often undetectable by even the most careful inspection.

That this disease really represents the early stage of invasive cancer has not been completely proved as yet, and indeed can only be shown by the careful following of a group of such cases over a period of years without treatment. That cancer of the cervix *may* arise in or follow carcinoma in situ has occasionally been shown without question. Younge, Hertig and Armstrong,[12] in a recent complete and careful article on the subject, cite 18 such patients reported in the literature. But to find cases of infiltrating carcinoma which follow carcinoma in situ is not the same thing as proving that carcinoma in situ is the *invariable* precursor of infiltrating cancer or that it turns into infiltrating cancer without exception if left untreated long enough.

In our own clinics, the conception that this is so, i.e., that cancer of the cervix begins as carcinoma in situ, is becoming more convincing as evidence collects. This impression rests on two principal observations, namely, that if one searches the cervical epithelium carefully enough by means of serial sections, one finds evidences of beginning infiltration in cases of carcinoma in situ in a fairly high percentage, and, second, if one studies sections of infiltrative cancer taken through the entire cervix or one entire cervical lip, one frequently finds carcinoma in situ in the mucosa beyond the margin of the infiltrative growth. Of 500 symptomless women studied by S. B. Gusberg chosen from the Group Clinic in Vanderbilt Clinic where they were being examined for some complaint other than a gynecological one, 10 showed intraepithelial carcinoma as picked up first by Papanicolaou smear and confirmed by biopsy. Of these, 5 showed beginning invasion of

* From the Department of Obstetrics and Gynecology of Columbia University and the Sloane Hospital for Women, and the New York City Cancer Institute. Presented at the Thirty-second Annual Meeting, American Radium Society, New York, N. Y., May 25–26, 1950.

the underlying stroma on careful study of serial sections from the surgically removed cervix.

If we assume, then, that carcinoma in situ is the first manifestation of cervical cancer, what is its duration? Does it progress slowly or rapidly if left untreated? Several authors have noted the difference in age incidence between carcinoma in situ and infiltrating carcinoma. TeLinde[10] found his patients averaged thirty-six years of age as compared with forty-eight for invasive cancer. The average age for 43 cases reported by Pund and Auerbach[8] was 36.6, while cancer patients averaged 48.6. Younge, Hertig and Armstrong[12] report an average age of 38.7 years in 135 cases and say this is 9.3 years less than the "accepted average age of 48 years for frank cervical cancer."

In the Pathological Laboratory of the Sloane Hospital, 60 cases of intraepithelial carcinoma have been seen. The age distribution of these cases is shown in Figure 1 where it is compared with the ages of 602 cases of infiltrative cervical cancer seen from 1917 to 1943. The youngest patient was twenty-seven; the oldest, seventy-one; the average age was 41.9. In the years 1948 and 1949, 94 primary cases of infiltrative cervical cancer were seen at the Sloane Hospital, the average age of which was 49.6.

All these figures suggest very clearly that there is a difference of eight to twelve years in the age incidence of in situ versus infiltrative carcinoma. Furthermore, if infiltrative carcinoma arises first as carcinoma in situ, it would seem that the latter exists for eight to twelve years before it becomes invasive. We appear to have a prolonged period of time on the average during which we may detect incipient cancer and treat it at our convenience with the prospect of close to 100 per cent cure.

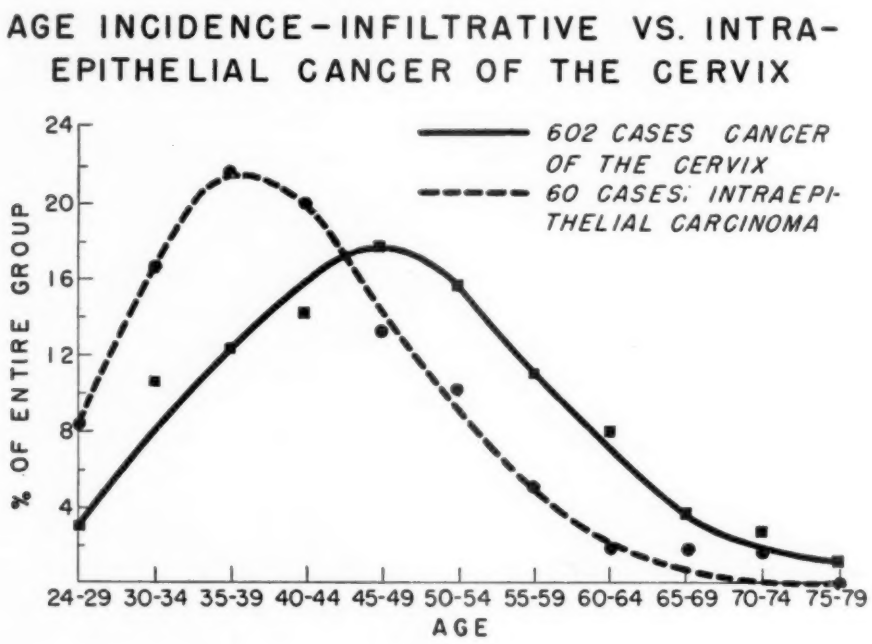

FIG. 1

Duration of Untreated Invasive Carcinoma of the Cervix. If intraepithelial carcinoma seems to be such a slowly progressive process, the question arises, Is this true for invasive cancer too? May our much vaunted results of radiation or surgical therapy be merely the expression of the natural history of the disease? Really to understand what we are accomplishing, it seems reasonable to compare our results as shown by the curve of the duration of life

of our treated cases with that of those who have received no therapy.

To obtain an answer to this question, the charts of 2,214 patients with cancer of the cervix seen at the New York Cancer Institute between the years 1930 and 1949 were reviewed. Among this number there were 171 who had received no surgical or radiation therapy, usually because they were in such poor condition or the disease was so far advanced when they were first seen that any attempt at curative therapy seemed useless. Of these, 114 were classified as League of Nations Stage IV; 51, Stage III; 5, Stage II; and 1, Stage I when first examined. Figure 2 shows the duration of symptoms in these patients from onset to death, as recorded in their histories. Surprisingly, once a woman develops symptoms of invasive cancer, usually vaginal bleeding or discharge, our studies seem to show that she will have a 50 per cent chance of dying in eleven months if she does not receive treatment. At the end of a year, 58 per cent of such women will be dead; at the end of two years, 82 per cent; and at the end of three years, 87.7 per cent. At five years only 4.6 per cent will be living. Invasive cancer of the cervix, untreated, is evidently a rapidly fatal disease in most cases, particularly in younger women.

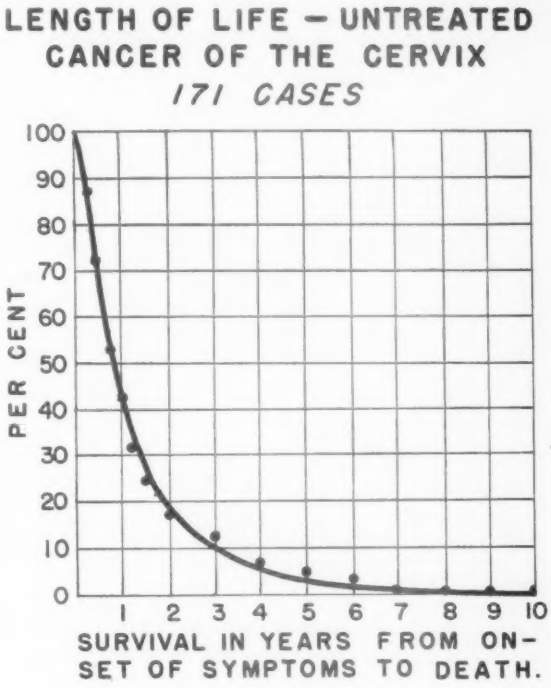

FIG. 2

Obviously the figures quoted above represent a very high degree of selection. In this day of widespread knowledge about

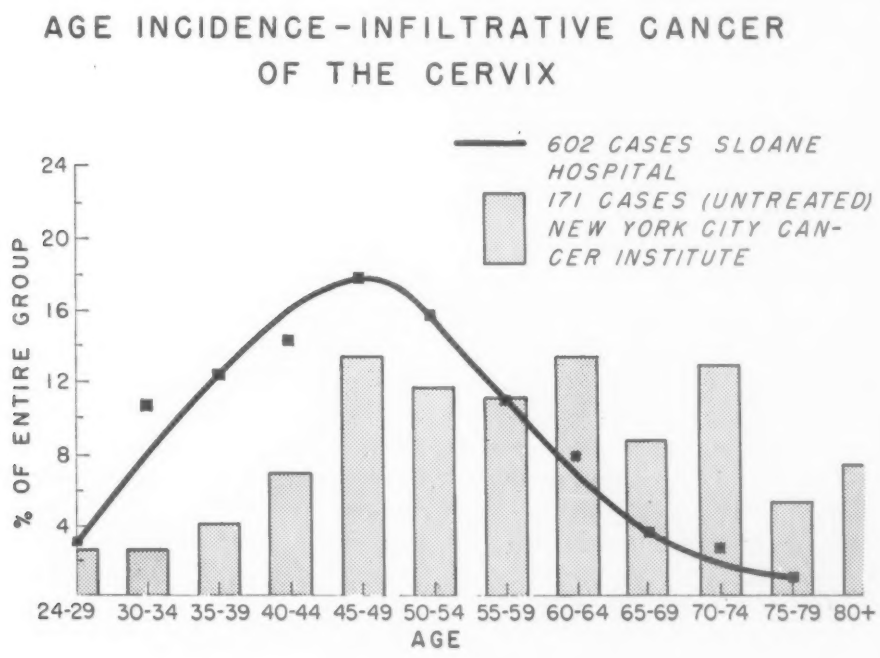

FIG. 3

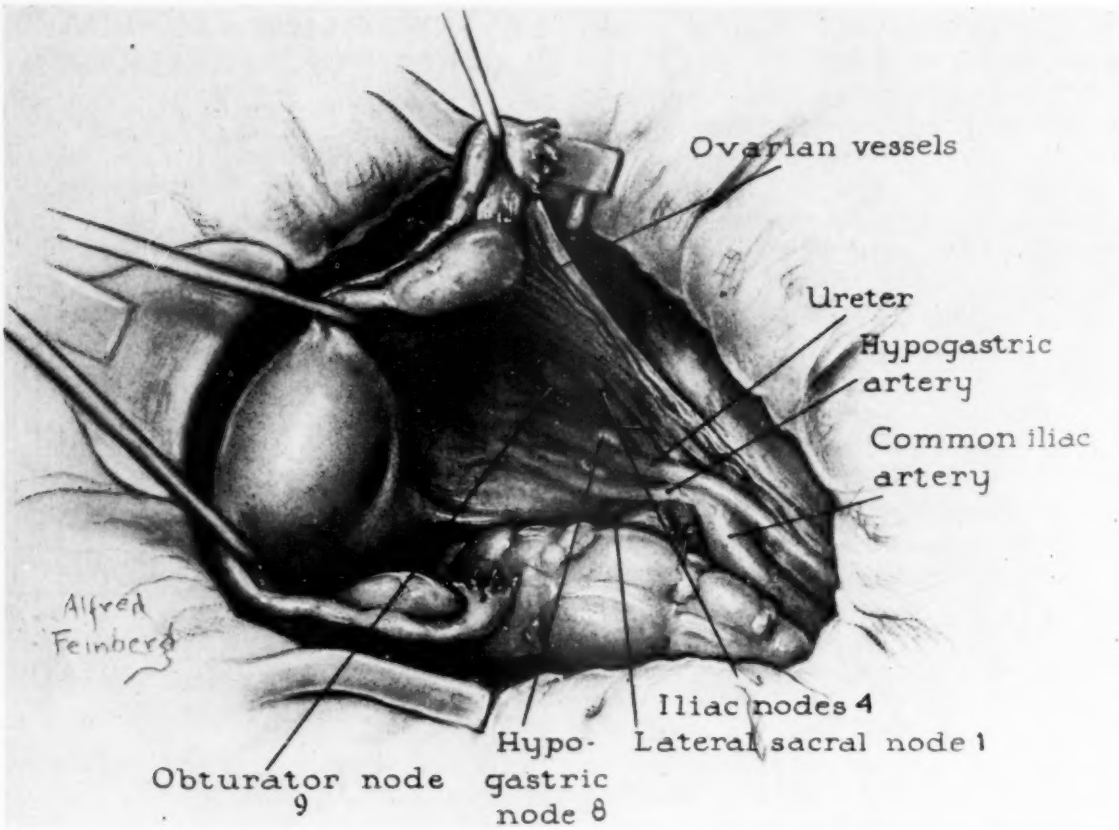

FIG. 4. Location of the primary lymph nodes on the wall of the pelvis. The broad ligament is depicted as being semitransparent to show the location of the underlying structures. The numbers after the names of the lymph nodes indicate the number of times in 91 radical hysterectomies for cancer of the cervix that each was involved with metastatic disease. (Reproduced by permission from *Cancer*, 1950, *3*, 975.)

cancer in New York City where free clinics are available for the indigent, 171 women dying of untreated cervical cancer must have done so because of extreme ignorance, fear, superstition, or neglect. The average age of the group is obviously older than for cancer of the cervix in general, namely 58.2. Figure 3 shows graphically this age distribution. Does the inclusion of so many older women in our group distort our curve for the duration of life after the appearance of symptoms? The answer is that it does, for if one calculates the duration of symptoms in the women in this group forty-nine years old or younger, the average is 10.2 months; for those between fifty and sixty-nine, an average of 22.6 months passed between onset of symptoms and death; and in those seventy or over, 14.8 months. From this we see that were it possible to study a group of women with cervical cancer similar in every way to those patients we see in our clinics daily, save that they were receiving no form of therapy for their disease, their death rate would probably be found to be even more rapid than that depicted in Figure 2.

This method of obtaining a base line for the natural course of untreated cancer against which one may project one's therapeutic results is not original with us, but has been done with 67 patients by Welch and Nathanson,[11] with 75 cases by Forbes,[3] and with 1,749 cases by Major Greenwood[4] for the British Ministry of Health. These reports seem to show a slightly longer duration of life, 5–6.5 months, than is shown in our material, again probably a result of selection.

Sites of Early Metastatic Spread. Since

Meigs[6] revived in this country radical hysterectomy as an accepted treatment of cancer of the cervix about ten years ago, this operation has been performed increasingly in various cancer hospitals and university clinics. Our first case was done in Feburary, 1944. Since that time, 91 patients have been so operated upon and the excised lymph nodes identified and studied for the presence of metastatic cancer.* In about half the cases, microscopic examination of the parametrial tissue outside the cervix showed invasion by cancer. Cancer in the regional lymph nodes, however, was found in only 15, or 16.5 per cent. It is evident that cancer of the cervix spreads by local extension into the parametria rather than by metastasis to the regional lymph nodes in most cases.

The groups of nodes involved in the 15 cases are shown in Figure 4, together with the number of times metastatic cancer was found in each. The nodes in the obturator fossa are the most common sites of metastasis, with the "hypogastric node," the lymph node lying in the bifurcation of the common iliac artery, coming next. The nodes along the external iliac artery are rarely the site of early metastasis, in our experience. When the iliac nodes are invaded, it is usually up near or above the origin of the hypogastric artery. In 1 patient, the lateral sacral node was removed during the course of a dissection of the sympathetic innervation of the uterus. This node proved to have metastatic cancer in it. The patient has remained well and apparently free of cancer some three and one-half years since. It is likely that this node represents one of the so-called primary group and receives drainage directly from the cervix via the lymphatics in the uterosacral ligament. As such it is possible that it is involved early with metastatic cancer more often than we realize and should be removed routinely in radical hysterectomies for cancer.

Sites of Late Metastatic Spread. Brunschwig and Pierce[2] have reported upon 65 cases of cancer of the cervix which came to autopsy at the Memorial Hospital from 1917 to 1948. Of these, 32, or slightly less than half, showed macroscopic evidence of the spread of cancer beyond the pelvis. In the Department of Pathology, College of Physicians and Surgeons of Columbia University, there are records of 33 autopsies on women with cancer of the cervix from 1916 to 1946. Of these, 16 had metastases outside the pelvis. The most common sites for such metastases were the periaortic or retroperitoneal lymph nodes. In the series reported by Brunschwig and Pierce, they were reported in 24 of the 32 cases. In the cases at Columbia, 12 of the 16 show this site of metastatic spread. Lungs and liver seemed to be the next most common areas. Bone metastases are rare except in the spine. A metastasis to the femur was reported once, as was a sacral metastasis. In 4 patients, vertebral metastases were found, but these were extensive in only two.

Henriksen[5] has studied the lymphatic spread of cancer of the cervix very carefully in two series of cases, the first consisting of 41 autopsies in which the lymph nodes or parametria were very carefully dissected, and a larger group of 315 in which only gross distinctions were made as to the location of lymph node metastases.

In the first group Henriksen divides the cases into 26 untreated patients and 15 treated ones. In the untreated group, there was parametrial spread of cancer in 77 per cent, involvement of the primary lymph nodes (obturator, hypogastric, and iliac) in 27 per cent to 31 per cent, and distant metastases in 27 per cent. In the treated cases, on the other hand, parametrial cancer had been somewhat controlled and was present in only 33 per cent of the cases. Primary lymph nodes were involved in 47 per cent to 67 per cent, and there were 33

* Fifty-three of these cases were operated upon at the Memorial Hospital for Cancer and Allied Diseases, New York City, between February, 1944, and September, 1948, by Dr. G. H. Twombly or Dr. H. C. Taylor, Jr. The remaining 38 have been done at the Sloane Hospital for Women, Columbia-Presbyterian Medical Center, New York City.

per cent periaortic lymph node metastases and 53 per cent distant metastases.

This suggestion that treatment of cancer of the cervix with roentgen rays and radium tends to control the disease locally and allows a longer time for distant metastases to occur is confirmed by Henriksen's larger series in which only 32.5 per cent had distant metastases, whereas in the treated cases 37.8 per cent had distant metastases.

Henriksen cites the liver as the most frequent site of distant metastasis, with bone, lung, and bowel following in that order. In his large series, 356 cases, the pelvis is not listed as ever having been involved. The most frequent site of bone metastasis was the vertebrae, 25 cases.

We may conclude that cancer of the cervix is a disease which is slow to metastasize widely, that it tends to kill its host by local changes in the pelvis, particularly ureteral obstruction and pelvic sepsis rather than widespread metastasis. Partial or complete control of the cancer in the cervix tends to give time for distant metastases to appear and grow and consequently to assume a more important role in the death of the patient. These distant metastases are apt to be to the periaortic nodes and the parenchymatous organs, liver, lungs, spleen, brain, etc. They also involve the spine fairly frequently, but hardly ever the bony pelvis. Cervical cancer differs radically in this respect from metastatic cancer of the breast.

The Cause of Death in Cancer of the Cervix. It is a generally accepted observation that the most common causes of death in cancer of the cervix arise as complications of ureteral obstruction. One of the best studies of this question was made a number of years ago by Auster and Sala[1] at the New York City Cancer Institute and Hospital. These authors studied 124 autopsy records, accumulated between the years 1927 and 1938, and in these cases they found "nephrogenic sepsis," i.e., pyelonephritis, pyonephrosis with hydronephrosis, cystitis, and ureteritis to be the chief cause of death in 23.3 per cent; uremia counted as the primary cause of death in another 4.8 per cent. As a secondary cause of death, damage to the urinary tract was present as hydronephrosis or pyonephrosis in 71.9 per cent of the cases. To quote from their paper, "These figures are startling in that they indicate lesions of the urinary tract to be the most important single specific influence in the downhill path of patients dying of cervix cancer for practically all of the patients in this study had some degree of urinary tract damage."

In Henriksen's study uremia was given as the cause of death in 58.5 per cent of the untreated cases and 49.3 per cent of the treated cases. Another 24.3 per cent of the untreated cases and 29.3 per cent of the treated cases had evidence of ureteral compression with hydronephrosis. Thus, 82.8 per cent of the untreated cases and 78.6 per cent of the treated cases had evidence of ureteral compression and kidney damage. In Brunschwig and Pierce's series, 41 of 65 had hydronephrosis.

Of the 33 autopsies done by the Pathological Department of the College of Physicians and Surgeons, 14 had ureteral obstruction or pyelonephritis secondary to it. In 10 this was the principal cause of death. Seven died of widespread metastatic cancer or its complications, 6 died of peritonitis, 2 of pneumonia, 2 of intestinal obstruction secondary to radiation therapy or carcinoma, 1 of radiation necrosis of the bowel, 1 of radiation necrosis of the bladder, 1 of uncontrollable vaginal hemorrhage, 1 of gangrenous cystitis and cachexia, and 2 of incidental causes unrelated to their cervical cancers.

It seems clear that with our present techniques of surgery and with antibiotics, it might be readily possible to change this picture materially. Urinary sepsis is uncontrollable chiefly when it is combined with ureteral obstruction. Transplantation of ureters to bowel or skin could decrease urinary tract fatalities, particularly if done early in the course of the disease, but there is serious question as to whether such a procedure would be worth while without

some new method of possible cure. Certainly to replace the relatively painless, often merciful death from uremia by a lingering, pain-wracked one from local extension of cancer into the sacral plexus or distant metastases might be a doubtful blessing even though it resulted in some prolongation of life.

SUMMARY

Cancer of the cervix uteri may begin as carcinoma in situ, a disease which has been detected by most workers in patients whose average age is eight to twelve years younger than that for women with infiltrative cancer of the cervix. If it can be shown that carcinoma in situ is the usual precursor of infiltrative cancer, these figures would suggest that we may have a prolonged period during which we may detect incipient cancer and treat it with the prospect of close to 100 per cent cure.

Untreated invasive cancer of the cervix, on the other hand, is a rapidly fatal disease, 58 per cent of patients dying within a year of the onset of symptoms and 82 per cent within two years. Four and six-tenths per cent of women with untreated cervical cancer survived five years.

Parametrial involvement occurs by direct extension fairly rapidly. In ninety-one patients treated by radical surgery, it was present in about half. Only fifteen, or 16.5 per cent, of these cases showed lymph node metastases. Nine had metastatic obturator nodes, eight had positive hypogastric nodes, and four had common iliac nodes.

Of patients dying of cancer of the cervix, only about one-half will show metastatic disease outside the pelvis. The most common sites of metastases are the periaortic and retroperitoneal nodes, the liver, the lung, and the vertebral column.

The commonest cause of death in cancer of the cervix uteri is either ureteral obstruction or infection of the urinary tract associated with it. Operative relief of such obstruction is of doubtful value, unless there is some promising method of curing the primary tumor.

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THE RESULTS OF SURGICAL TREATMENT OF CANCER OF THE CERVIX UTERI*

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THE invitation to present this material is slightly premature. A report of surgical progress should not be given before at least 100 patients have been followed for five years. Next year (1951) 100 patients radically operated upon with cancer of the cervix uteri will be reported with a five year follow-up. The results of the node dissections are incomplete and at this writing 80 patients will be reported and 46 of these will have been followed for three years or more. The first part of this report is based upon the five year results of 75 patients (Table 1) operated upon by radical hysterectomy and bilateral pelvic lymph node dissections. Inasmuch as these results seem to follow the five year report of 54 patients very closely it is a real indication of what may be expected in the first 100 patients.

TABLE I

75 RADICAL OPERATIONS

Living—59, or 78.7%	Positive lymph nodes—4
Dead—16, or 21.3%	Positive lymph nodes—10
Postoperative deaths—0	

The results are good, but it must be remembered that these patients were selected from our Stage I and Stage II material. If these results could be projected upon all the Stages I and II there is no doubt but that the radical surgical treatment would have a large place in the treatment of this disease. There is no doubt that local recurrences are rare, injuries to bowel absent, lymph node extensions curable, and although ureteral injuries were caused in the first surgical attempts they have been increasingly more and more infrequent. We find that the surgical treatment is less taxing to the patient, from both the discomfort and the economic side. The only problem at the moment is the occasional difficulty encountered in voluntary voiding. In some instances there will be difficulty starting, and scheduled voiding must take place as sensation is done away with. This discomfort has been more and more evident in the last cases where the operation has been extended as experience develops and the surgery becomes more complete.

There are very few reasons for avoiding surgery in the early stages but it is my observation that unless the surgeon has acquainted himself with the operation he should rely upon irradiation. This is not the time to advocate surgery for all who have this disease and it is not my desire to advise surgery in any case of cervical cancer. That it has been done with excellent results may be indication of a trend, but this trend will end in many disasters unless thought and care are put into the selection of cases and especially the selection of the operator.

It is obvious that since surgery has been suggested as a means of treatment the number of surgical disasters and surgical mistreatments have been out of all proportion to the value gained from the poorly considered surgical attack. For the time being and until a very large series has been reported at five years, we must all definitely advocate the use of radium and roentgen irradiation as the treatment of this disease. This cannot be emphasized too strongly, *yet* I have been asked by this Society to present the surgical results and although I do so, it is with considerable hesitancy. The American Radium Society should be aware of the progress that is being made in the surgical attack upon the

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disease, just as the surgical groups should be informed about the irradiation results. However, it should be the duty of your Society to minimize the surgical results at the present time and to emphasize the great number of cures obtained by irradiation. Some day a large number of figures from a clinic will be presented to compare with the irradiation results and then, without doubt, surgery will come into its own in the treatment of this disease. The most important aim should be to find the means to evaluate radiation sensitivity from radiation resistance. That there is such a difference can be no longer denied. The mere viewing of the disasters at Hiroshima and Nagasaki should make it clear to all that these phenomena exist. Ruth Graham[2,3] has ably demonstrated the possibility of distinguishing one from the other and Glücksmann and Spear[1] have shown the way to establish an index of malignancy. This latter work has not been proved over a long enough period as yet but any attempt to demonstrate the resistance and sensitivity of a patient or tumor is of the greatest importance. It will then develop that certain patients will be irradiated and certain others will be surgically treated. This is the acme of our desires and interests. There have been various investigators who have cited this problem and, because of their work, selection will eventually be possible. It is not my belief that more, better, or stronger radiation is the answer but selection for sensitivity and resistance. The results of the best radiation therapy clinics are nearly the same and a further approach must come along the lines of selectivity and not just better radiation application.

Location of the areas of lymph node extension, by means of marking with dura clips as suggested by Dr. Langdon Parsons, and location of the extent of the tumor itself in the pelvis, as done at the Vincent Memorial Hospital, will surprise the radiologist when he sees these areas outlined. Stereoscopic views of the pelvis with marked lymph node areas demonstrate the great difficulty of applying lethal radiation to those areas. Marking the extent of the local pelvic spread will provoke the radiologist into thinking further about methods of radiation treatment. Certainly no model or drawing will demonstrate the disease and its extension as well as films of the clipped areas of extension as shown following operation. The mere packing of the vagina with gauze displaces the vaginal apex and the cervix and makes attempted reconstruction of the upper vagina, cervix, and parametrium incorrect. The parauterine tissue is not of any consequence, but the paracervical and paravaginal tissues are important, and tight vaginal packing displaces applicators, needles, and other apparatus used in treatment. There must be a better understanding of the spread and a change in the methods of radium treatment, and it is my opinion that a radiologist well versed in surgery or a surgeon well versed in radiation therapy would be of the greatest help in the treatment of cancer. Neither surgery nor irradiation by itself is the only method of treating cervical cancer and yet a combination of these treatments is not good, but a selection of cases for either one method or the other is of the greatest importance at present.

MATERIAL

The material in this report constitutes the first 75 patients operated upon by the author since 1939. At that time we did 2 patients each year and it was not until 1942 that our patients averaged 20 per year. It took until 1950 to be able to review the 75 patients and to follow each one for five years. Though we have done radical operations for cancer in situ, cancers in situ have all been excluded from this report. We believe that this material from the Massachusetts General Hospital, the Vincent Memorial Hospital, the Pondville Hospital (Massachusetts Department of Public Health), and the Palmer Memorial Hospital is a satisfactory example of what surgery in ideal circumstances may accomplish for patients with this disease. The patients were selected for their youth,

slenderness, good health, and normal physiologic and chemical findings. That more could have been operated upon there is no doubt. At the present time our Staff is operating upon more that 50 per cent of all patients coming to the clinic. This indicates that the number of patients to treat radiologically in our clinic has fallen. This is a large surgical experiment and it is our hope that our radiologists will bear with us until it can be established which is the proper method of treatment.

In this report only Stage I and Stage II patients are included, and the staging was done on the first visit and not at operation. Findings at operation did not change a clinical Stage I to Stage III, nor did distal lymph node involvement change the stage to Stage IV. Strangely enough, figures show that the clinical staging was satisfactory, for the Stage I cases did better than the Stage II, both as to results and as to lymph node involvement. As our experience increased, more patients were operated upon and the indications for operation were enlarged. The most important lesson learned from the surgery was increased knowledge of the anatomy of the pelvis.

TREATMENT

The treatment of these 75 patients was primarily surgical. In some with proliferative growth that we feared might recur due to spillage of tumor in the operative field, preliminary radium and roentgen treatments were given. The figures show that the best results occurred in the non-irradiated cases and these were most often the ulcerative or invasive type, as contrasted to the less malignant, proliferative type that received preoperative irradiation. The surgical treatment consisted of the abdominal approach to the cancer, an attempt was made to remove—so far as possible—all the lymph nodes, lymph channels and fat from the common iliac artery down along the whole arterial and venous tree into the pelvis, beneath the bladder, around the rectum, into the obturator fossa, and wherever material could be removed. It is our aim to bare the pelvic walls and to remove as far as possible the most important paracervical and especially paravaginal fat, lymph nodes, and lymph channels. This is not a block dissection but is as near to one as possible.

Roentgen or radium treatment, if used, was given in small amounts. In only a few cases was complete radium and roentgen treatment given. For the past two years we have avoided the use of irradiation in the surgical patient, except in instances for research. It is our feeling that irradiation and surgery do not go together and that a firm, hard, fixed pelvis results from combining the two. It is often possible, on examination of a patient after operation, to tell by the "feel" whether she has had radiation treatment in addition to surgery. Fibrosis, sclerosis, and induration occur following irradiation and this sort of change in the pelvic tissue should not be mixed with surgery. If a full dose of radiation is given, the patient receives 4,000–5,000 milligram hours of radium in the cervix by intracervical application and interstitial needles plus 8,000–12,000 r by means of a 200, 400, or 1,000 kv. roentgen-ray machine. If one-half the dose is given, the patient receives 2,000 milligram hours of radium in and about the cervix and 4,000–6,000 r from the above mentioned roentgen-ray machines directed to the parauterine cervical and vaginal areas, or crossfiring the cervix. In some instances, only one-half the dose of radium was given and in others one-half the dose of roentgen radiation chosen. A separation of the irradiated patients from the 75 cases will be presented later, for this Society should be especially interested in the accurate findings of our study, inasmuch as in 27 cases pelvic surgery followed the various types of radiation treatment.

THE LYMPH NODES

The lymph nodes of the pelvis, and no claim is made that all the lymph nodes or lymph channels of the pelvis are removed at operation, are dissected as carefully as

possible, starting well up on the common iliac artery and continuing the dissection into the depth of the pelvis. At operation, each chain of lymph nodes, common ilac, external iliac, internal iliac (or hypogastric), obturator, and ureteral, is placed in separate containers for examination by the pathologist. The paracervical and paravaginal tissues are carefully inspected by the pathologist and selected areas placed in solution for section. In the surgical procedure the pelvis is well denuded, but obviously not completely, of lymph nodes and lymph channels. In 14 patients, or 18.7 per cent of 75 cases, lymph nodes were found that were proved to contain cancer. Unquestionably, if serial sections were done on all nodes more positive areas would have been found, but the time and effort of the pathologist must be taken into consideration. Much more personnel and money would be necessary for a perfect study. The location of the nodes in these 14 patients is shown in Table II. Of this group, it is a great satisfaction to report that 4, or 28.6 per cent, are living at five years. Taussig and Bonney both reported that 20 per cent of their patients with positive lymph nodes would survive five years following their operative procedures.

Table II

DISTRIBUTION OF LYMPH NODES

	Living	Dead	Total
Iliac	2	5	7
Obturator	2	6	8
Ureteral	—	1	1
	—	—	—
	4	12	16

1 case—obturator and ureteral
1 case—obturator and iliac
(1 with positive tube living)

Lymph node involvement is not always clear to the operator and in some patients large nodes proved to be negative while small ones proved to be positive. If lymph nodes can be felt running up along the aorta it is not wise to continue with a radical operation for this finding means inoperability. It is generally felt that irradiation will not destroy positive nodes in cervical cancer. This is not possible to prove, but if it can be assumed that this is true it is important that 4 of 75 patients were salvaged by the surgery.

IRRADIATED CASES

In this group of 75 patients, there were 27, or 36 per cent, who were irradiated by one of the methods described above (Table III). Of these 27 patients, 19 are living, or 70.4 per cent of the irradiated patients. This must be compared with 83.3 per cent of the 48 patients who did not have any radiation treatment. In the irradiated group who are living, 5 are considered by us to have had adequate radiation treatment. Two had full roentgen-ray and radium, 2 had full radium, and 1 had full radium and one-half of the usual roentgen treatment. Of these 5 cases, 3 showed no cancer in the cervix removed at operation and 2 had cancer present at operation. One of these patients following full radium treatment had positive lymph nodes at the time of operation, in addition to cancer being present in the cervix.

Table III

IRRADIATION (FULL OR PARTIAL)

No. Cases	27, or 36.0%, of 75 cases
Nodes	7, or 26.0%, of 27 cases
Fistula	2, or 7.4%, of 27 cases
Dead	8, or 29.6%, of 27 cases
Living	19, or 70.4%, of 27 cases

Of those living who had a dose of one-half the usual amount of roentgen treatment and one-half the usual radium treatment in an attempt to reduce the size of the local lesion or to attenuate it so as to avoid implantation at the time of surgery, 3 were without cancer at operation and 3 had cancer remaining in the cervix. In 1 patient who was given one-half of the usual radium treatment no cancer was found in the cervix at operation. Of 3 with full roentgen treatment but no radium, all had cancer remaining in the cervix and 1 had positive lymph nodes, but, strangely enough, among 4 patients with only one-

half the usual roentgen treatment and no radium at all, 2 were without cancer in the cervix and 2 with cancer. All of this tends to demonstrate that radiation sensitivity and resistance are real problems to contend with and should point the way, to those interested in the study of cancer, to the importance of sensitivity of cancer cells to irradiation.

In the living group of irradiated patients, of 12 Stage I cases 7 had no cancer at operation, and 2 in 7 Stage II cases. In the living Stage I cases without cancer being found at operation adequate treatment was given to 2, and in Stage II adequate treatment was given to only one. In other words, only 3 of 9 patients found at operation to be without cancer in the cervix were given adequate treatment. Radiation treatment is very difficult to evaluate, as these figures so definitely show.

Analysis of the 8 cases, who were treated by irradiation and surgery and who died, shows that of 3 Stage I patients 2 died having distant metastases and positive lymphs nodes. One died four and a half years after operation of hypertensive heart disease and no lymph nodes were present. In Stage II 5 patients had irradiation and 3 died of distant extension who had positive lymph nodes, 1 died of distant extension whose lymph nodes were negative and 1 died of meningitis at two years, whose lymph nodes were negative. The most significant finding and one very favorable to irradiation, though it is acknowledged that an insufficient number of cases has been studied, is that no patient in this irradiated group died with local disease present. This is important and should be emphasized. It is evident that radiation was given in very varied amounts and that in only 6 patients was the dose considered adequate. Two patients with positive lymph nodes who survived and who had had irradiation both had inadequate radiation therapy for their lymph nodes—1 had no roentgen treatment and 1 had no radium. In the irradiated group of 27 cases, lymph nodes were positive in 7, or 26.0 per cent, and 2 survived; 1 had inadequate irradiation and 1 full radium and no roentgen treatment.

NON-IRRADIATED GROUP

It is important that we analyze the non-irradiated group of 48 patients who have been followed for five years (Table IV).

TABLE IV

NO RADIATION TREATMENT

No. Cases	48, or 64.0%, of 75 cases
Nodes	7, or 14.6%, of 48 cases
Fistula	8, or 16.7%, of 48 cases
Dead	8, or 16.7%, of 48 cases
Living	40, or 83.3%, of 48 cases

Forty, or 83.3 per cent, are living five years. Seven, or 14.6 per cent, had positive lymph nodes, a smaller percentage than in the irradiated group. Of the 8 deaths, 4 were in Stage I and 4 in Stage II. Of the 4 deaths in Stage I, 2 died of distant extension, with positive lymph nodes, and 2 died of intercurrent disease with negative nodes. In Stage II, 3 died with local vaginal disease present, 2 with positive lymph nodes and 1 without, and 1 died of distant metastases who had positive lymph nodes. (It should be pointed out here that the incidence of ureterovaginal fistula was higher, 16.7 per cent in the non-irradiated group than in the irradiated group, 7.4 per cent.) The results of the treatment in the non-irradiated group were superior to the irradiated group, being 83.3 per cent "cures" to 70.4 per cent "cures." These figures cannot be given too great significance for the numbers are small, yet the same trend has been present throughout the analysis of this series.

RESULTS

The results in the group of 75 patients treated by means of radical abdominal hysterectomy with bilateral lymph node dissection are of great interest. These patients, the first 75 operated upon in our hospitals, were selected because they were younger, thinner, and in better physical condition than the whole group of Stage I and Stage II patients. Whereas the first cases were selected carefully, the surgical

selections at the present time are less stringent and age and weight do not count so much. The results are so good in these cases that if it were possible to project the surgical treatment in all Stage I and II cases it is obvious that it would be done. Seventy-five patients were operated upon five years ago or more. Five years after the operation 59, or 78.7 per cent, are living and well. Breaking the stages into Stages I and II (Table V) shows that in Stage I 86.3 per cent are living and that 62.5 per cent of patients in Stage II are living and well. In this group of patients 14, or 18.7 per cent, had positive lymph nodes and 4,

TABLE V

Stage	Living	Lymph Nodes Positive
I—51	44, or 86.3%	3
II—24	15, or 62.5%	1

or 28.6 per cent, of these patients are living. Taussig and Bonney both found in their groups that were subjected to surgery that about 20 per cent of these patients with positive lymph nodes lived five years. The cure of patients with positive lymph nodes is most important for without surgery they surely would have died, as irradiation is ineffective against lymph node involvement. In Stage II the number of patients with lymph node involvement is 29.1 per cent. The grades of tumor are of considerable interest (Table VI), for in Grade I no patients had positive lymph nodes and 85.7 per cent are living. In the Grade 2 cases, 19 per cent had positive lymph nodes, and in the Grade 3 cases, 26.7 per cent. Six adenocarcinomas had 33.3 per cent of positive lymph nodes. The Grade I cases did best and the Grade 2 and 3 about the same at the end of five years. In the surgical group no patient died after two years who did not have positive nodes or die of intercurrent disease.

The figures so far presented include all cases, but of this group 4 died of intercurrent disease; I died of cancer of the bronchus and no cervical tumor was found at autopsy; I died of cancer of the stomach and no cervical tumor was found at autopsy; I died at two and a half years of meningitis; and I died of hypertensive heart disease at four and a half years. None of the 4 patients had positive lymph nodes. The chance of their surviving with cancer for five years was very great, especially so as no patient without positive lymph nodes died after two years. If these 4 patients could be excluded, the survival rate at five years would be 83 per cent. There is no doubt that this would be a fair exclusion but, even without doing so and using the absolute cure rate figure of 78.7 per cent, great encouragement is given to those interested in the treatment of cervical cancer. In Stage I, 3 patients are living who had positive lymph nodes at the time of operation and in Stage II one patient is living who had positive nodes. One of the Stage I patients after adequate radium treatment and with positive nodes and I of the Stage II patients with full roentgen

TABLE VI

Grade	Per Cent of Entire Group	Living	Positive Lymph Nodes Per Cent
1	7— 9.3%	6— 85.7%	—
2	21— 28.0%	15— 71.4%	19.0%
3	30— 40.0%	22— 73.3%	26.7%
4	2— 2.7%	2—100.0%	—
Adenocarcinoma	6— 8.0%	5— 83.3%	33.3%
A.A.	2— 2.7%	2—100.0%	—
? grade	7— 9.3%	7—100.0%	—
	75—100.0%	59— 78.7%	18.7%

treatment with positive nodes are living five years. Both had cancer remaining in the cervix. Two Stage I patients with positive lymph nodes living five years had no irradiation and had cancer in the cervix at operation.

REGION OF RECURRENCE

Dividing the 16 deaths into stages, in Stage I it was found that 4 died of distant extension of the disease, all with positive

lymph nodes and 3 died of intercurrent disease, with negative lymph nodes. In Stage I, excluding those who died of intercurrent disease but 4 succumbed to the actual disease and all of distant metastases. The results in Stage I, omitting those dying of intercurrent disease, could be 91.6 per cent and in Stage II, 65.2 per cent survival. These last figures are not absolute; nevertheless it is well to mention them, assuming that the 4 patients dying of intercurrent disease could be excluded. The cause of death is, in the main, extensive involvement with disease, death being due to uremia, intestinal obstruction, pulmonary lesions, carcinomatosis, and cachexia.

URETERS AND KIDNEYS

Ten, or 13.3 per cent of our operative patients, developed ureterovaginal fistulas (Table VII). This is distressing but in the later groups operated upon, this incidence has been markedly decreased so that at the present time this complication is not one to be looked for as it was in the first cases. There will always be an occasional fistula but, on the whole, the number should not be too great. There have been only 2 nephrectomies and in 7 instances the fistula has healed with loss of the kidney and in some, healing has taken place with establishment of continuity of the ureter. One patient with a huge tumor had bilateral fistulas and died six months following her operation. Recently transplantation of the ureter to the bladder has been successful and it is obvious that the ureteral problem has a good chance to be solved. Salvage of arterial blood supply to the ureter, preservation of the longitudinal blood supply of the ureter and attempts to leave the ureter on the peritoneum for as long a distance as possible will help to preserve the ureter intact. Fifteen cases had recent intravenous pyelograms which showed that from four to nine and a half years later damage to the kidneys and ureters was minimal after surgery. These 15 cases show conclusively that late damage to ureter and kidney following this operation need not be expected. On the whole, with but 1 death six months after operation, due to operative ureteral damage and with only 2 nephrectomies being necessary, the ureteral problem is not too serious or important to mitigate against surgery. In radiation treatment there is nearly the same possibility of injury of ureter, bladder, and kidney.

TABLE VII

Ureteral fistula—10 (13.3%)	
Kidney removed	2
Healed without surgery	7
Died 6 months—bilateral fistulas	1

DISCUSSION

A discussion of the problem of treatment of cancer of the cervix based upon the results of only 75 operated patients is not conclusive. Suffice it to say that surgery can be done with a great degree of safety. No patient died a postoperative death. This had to be demonstrated before surgery could be entertained as a method of treatment. Roentgen therapy appears to be of value in preventing local recurrence of the disease in surgical patients. It is true that the more advanced the disease, the less the hope of cure. Stage I, Grade I cases do better than all others, but in Stage II or in Grades 2, 3, and 4, good results can be expected. Better results will be obtained when different investigators, and especially pathologists, point out to us radiation sensitive or radiation resistant patients or cancers and help us to decide the cases to be operated upon and those to be irradiated. Unquestionably this will be decided in the future. Through histochemical methods, the observation of the cytologists, the work of tumor transplantation, and other investigations, unnecessary surgery and unnecessary irradiation will be avoided. We have all seen similar cancers destroy one patient and be cured in another. There must be individual protection and individual lack of resistance against cancer, just as there must be direct invasive and/or metastasizing and rapidly spreading cancer.

Solving of such problems will be of the greatest help to all of us interested in this disease. Such work should be stimulated and carried out wherever possible, for large and destructive surgical operations, although life saving in certain circumstances, are to be deplored if sufficient help can be obtained from the above groups of investigators to demonstrate to us as radiotherapists and surgeons our proper procedure upon an individual with cancer.

Conclusions. This small group of cases operated upon by a radical abdominal approach, with removal of the uterus, paracervical, and paravaginal tissue with no mortality, gives a remarkable percentage of cure of the disease. It is a selected group, yet all patients had invasive cancer; some patients were irradiated and some not, but all in all, the survival figures are so satisfactory that it is our hope that larger groups of patients will show the same successful trend.

TRANSPERITONEAL NODE DISSECTION (TAUSSIG) AND RETROPERITONEAL NODE DISSECTION (NATHANSON)

Transperitoneal Node Dissection (Taussig). The late Dr. Frederic J. Taussig of St. Louis advocated a transperitoneal approach and removal of pelvic lymph nodes in patients with cancer of the cervix. It was his belief that cancer in the lymph nodes would not be cured by irradiation and he therefore thought that removal of nodes in the area of cervical cancer spread might greatly increase the chance of cure in this disease. His first paper on the subject in 1934 and his subsequent writings and advice suggested that his operation offered a definite chance for cure in certain patients. No doubt this surgical attack in addition to irradiation offered more than irradiation alone.

This operation is done upon patients who have had complete and satisfactory radiation treatment, if the surgeon believes that by dissecting out the pelvic lymph nodes the patient will have a better chance of cure. In some instances where a total hysterectomy or vaginal hysterectomy has been done and where cancer was found in the removed specimen, a dissection of the nodes may be preferred to a radical operation with removal of the remaining vagina and paravaginal tissue plus lymph node dissection. The operation consists of a dissection of the common iliac artery and veins, and the arterial and venous trees down into the pelvis, to the obturator fossa, the tissue about the uterine artery-ureter crossing and the lymph node, lymph channel bearing tissues about the bladder and rectum as far as possible. This operation cannot be nearly as extensive as the pelvic dissection done at the time of the radical operation with bilateral pelvic lymph node removal. The uterine artery is exposed and may be tied off but the ureter is not dissected from its groove about the low cervix and upper vagina. This operation is not a perfect cancer operation but does take care of most of the lymph node spread in the pelvis. It misses, however, the paracervical and paravaginal tissues. This operation was undertaken in our clinics about the same time that the radical operation was instituted and one of its faults lay in the temptation to the surgeon to do the radical operation, once the pelvis was entered and explored. Because of the great difficulty in evaluating the irradiated cervix the surgeon, as long as the nodal dissection went well, was considerably tempted to remove the uterus and surrounding tissues. After performing this operation 11 times it has practically been given up. Dr. Taussig in his reasons for doing the operation completely ignored the state of the cervix for he felt that it was essential to remove the nodes whether or not the local disease was cured. If it was cured nodal removal would have been done and if it was not cured no harm had been done.

A follow-up is available for 11 Taussig operations for three years and eight months to over five years (Table VIII). To our delight 2 patients in this group are living for five years and nine months each. In the 11

cases 6 are dead; 3 of the 11 had positive lymph nodes. In 1 who had positive lymph nodes, the location of the lethal disease was not known; in 2 pelvic extension was fatal; in 1 a metastatic lesion in the lung was the cause of death; in 1 pelvic and bony extension were present at death; and in 1 the disease was local as well as pelvic. In all 6 deaths the treatment before surgery was irradiation.

TABLE VIII

	Retroperitoneal	Taussig
Number	69	11
Positive lymph nodes	16—23.2%	3—27.3%
3 year cases	35	8 (5 years)
Positive lymph nodes	7—20%	3—37.5%
Living with positive lymph nodes	—	2

The cases were divided into stages and grades. There were 3 Stage I patients and 3 are living—1 with positive lymph nodes following simple total hysterectomy—who have survived five years. In Stage II there were 4 patients and 1 is living who had negative lymph nodes. In Stage III of 2 patients, 1 is living who had positive lymph nodes. Of the 2 secondary cases neither is living; 1 had positive lymph nodes.

Of 8 patients at five years, 2 of 3 with positive lymph nodes are living five plus years; this indicates that this operation must be taken more seriously and that perhaps greater use should be made of its possibilities. There have been no postoperative deaths and no surgical calamities.

Retroperitoneal Lymph Node Dissection (Nathanson). In May, 1945, Dr. Ira T. Nathanson of Boston carried out the first retroperitoneal dissection of the pelvic lymph nodes for cancer of the cervix at the Pondville Hospital (Massachusetts Department of Public Health). Since that time this operation has been performed many times at the Massachusetts General Hospital, the Vincent Memorial Hospital, the Pondville Hospital (Massachusetts Department of Public Health), and the Palmer Memorial Hospital by members of the Gynecologic Staff of these hospitals and by residents in these hospitals. The operation is quite safe and only 2 calamities have occurred in the series reported here. In 1 case on the wards of the Massachusetts General Hospital spasm occurred in the femoral artery during removal of lymph nodes from that area. Relief of the spasm could not be obtained and the patient eventually lost her leg due to gangrene. In another patient, death occurred three days after operation from a pulmonary embolus. This operation has been done 69 times (Table VIII) in our institutions, all by members of the same gynecologic group and their residents.

The operation consists of a bilateral retroperitoneal dissection of the nodes of the common iliac artery and vein, down the arterial and venous tree, into the region of the uterine artery and ureteral crossing, dissecting the obturator fossa clean, and removing all the lymph nodes and channels and fat in this area. The operation can be done more easily than the Taussig operation and can be done in stages in the less favorable surgical risk. The temptation to remove the uterus, cervix, and vagina is not present. This exposure is as satisfactory as the Taussig procedure but here again the paracervical and paravaginal tissues are not satisfactorily cleared out and reliance is placed upon irradiation to care for these areas. As in the Taussig operation, the fate of the cervical lesion cannot be known and although biopsy and vaginal smears suggest a destruction of the cancer, local recurrence may easily happen and the operation —no matter how well done and no matter how many nodes are removed—cannot be successful.

To prove the success or value of this operation, some patients with local cure and positive lymph nodes must be salvaged for five years or more. Unfortunately, this has not been the case, but 1 patient went for three and a half years who had a positive lymph node. Two Taussig operations

in patients with positive nodes have cured the patients for nearly six years—a definite suggestion that with better treatment of the local lesion some patients will be cured. Among the deaths there were 12 patients with positive lymph nodes and a local cure was not secured in two. Local persisting disease therefore was responsible for some failures. In 2 others without positive lymph nodes local disease was responsible. Direct extension into the pelvis, into unremoved nodes, into bone, and into pelvic tissue was responsible for most failures.

Of the total of 69 patients, 23.2 per cent had positive nodes—a slightly higher percentage than found in the radical operation cases. Forty-six of the 69 patients are living at the present time and 8.7 per cent of them had positive nodes. The follow-up in many cases is under three years. The distribution of positive nodes is about as in the cases with radical surgery, though more seemed to have more than one region involved. Stages I and II comprised the great majority of patients subjected to this operation. There were 51 patients in the two groups and of the 51, 72.5 per cent are living. Of this group of 51 patients 10, or 19.6 per cent, had positive lymph nodes —a figure of nodal involvement very similar to the percentage found in the radical operation. In the rest of the group 33.3 per cent had positive nodes but this group is too small to calculate with any degree of accuracy. Most of the patients in this group were treated previously by satisfactory roentgen and radium treatment. It is my belief that this surgical procedure will eventually prove to be a satisfactory operative measure when the local lesion can be definitely destroyed.

When the retroperitoneal lymph node dissections are studied at the three year mark, it is found that 1 patient lived three and a half years with positive nodes and then died, but that all other patients with lymph node involvement died earlier. Thirty-five patients were operated upon three or more years ago and 21 are living and 14 are dead.

DISCUSSION

It would seem to me that there is very little to choose from between the retroperitoneal dissection of nodes and the Taussig method. It is evident that a few patients with positive lymph nodes may be salvaged but that with so many dying of persistent, invasive, and metastasizing disease we must look to our laboratory investigators for clues as to who should and who should not be subjected to irradiation or surgery.

Combining the five year results of the Taussig and radical operations, as far as lymph node involvement is concerned, there was a total of 83 patients and 17, or 20.4 per cent, had positive lymph nodes. Of the 17 patients with positive lymph nodes 6, or 35.2 per cent, have survived for five years. This is encouraging but the figures are so small in number that they will be in all probability changed in future analyses. However, to be able to cure any patient who had positive lymph nodes indicates that such a procedure is wise and probably necessary.

TABLE IX

	No.	Positive Lymph Nodes
Retroperitoneal lymph nodes	69	16
Irradiation	65	15—23.0%
No irradiation	4	1—25.0%
Taussig's operation	11	3
Irradiation	8	2—25.0%
No irradiation	3	1—33.3%
Radical hysterectomies	75	14
Irradiation	27	7—26.0%
No irradiation	48	7—14.6%
All types of operation	155	33
Irradiation	100	24—24.0%
No irradiation	55	9—16.4%

There are 155 patients reported in this paper (Table IX), including those operated upon by the radical operation with bilateral lymph node dissection, the Taussig operation, and the Nathanson operation. Of these 155 patients 100 had irradiation and 24, or 24 per cent, had positive lymph nodes. Fifty-five were given no radiation treatment and but 9, or 16.4 per cent, had positive lymph nodes. There is no indication here that irradiation diminishes the number of positive lymph nodes found at operation.

CONCLUSIONS

1. Surgery can be done upon patients with cancer of the cervix with comparative safety.

2. Selection of cases is not necessary for by means of one of these procedures most can be given a chance for cure, as far as lymph nodes are concerned.

3. Irradiation before radical surgery may help prevent recurrence of local disease.

4. Destruction of local disease must be complete before any results can be expected in the Taussig or Nathanson operation.

5. The results fully justify surgery, but the number of cases is so few that the whole plan should still be considered as experimental.

6. Aid is needed from various types of laboratory investigation to help decide which patients should be operated upon and which should receive radiation therapy.*

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* For discussion see page 722.

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RADIATION TREATMENT OF CANCER OF THE CERVIX UTERI*

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INTRODUCTION

THE topic assigned for discussion in this portion of the Symposium on Carcinoma of the Uterine Cervix concerns the technique of radiation therapy on the basis of dosimetry. Certainly, there is neither the time nor the necessity for a comprehensive and detailed account of all the treatment methods employed. However, it may be of interest to review briefly some of the principles upon which irradiation techniques are based and to investigate the possible value of technical improvement.

At the outset it must be emphasized that radiation therapy for carcinoma of the uterine cervix was first developed on the basis of empiricism. Biological and physical experimentation necessary for the evaluation of the processes involved lags behind. Numerical expressions, such as dosage calculations or survival statistics, still seem somewhat removed from the specific problem of a human subject harboring this type of tumor. On the other hand, we cannot depend entirely upon our own experience, or even the reported experiences of others, to give us reasons for our apparent successes or failures in the treatment of this disease. We will need more experimental information concerning the biological processes involved before we can completely evaluate our clinical impressions. However, we cannot help but attempt to correlate what we do believe are basic principles with what we currently observe.

PART I

Ionizing radiations must be traumatic to tissue by their very nature. This trauma may manifest itself through one or more theoretical mechanisms, but certainly the local biological reactions are similar to reactions to other injurious agents. It is an accepted theory that the effects of such radiations are motivated on the basis of a differential recovery rate between normal and more susceptible tissue. In the treatment of carcinoma of the cervix uteri there is a minimum amount of radiation needed to control the growth of the existing tumor and a maximum amount which will cause irreparable damage to normal structures of the tumor bed. It is theoretically best to deliver a uniform amount of radiation throughout the entire area of possible involvement by the tumor so that the minimum dose may be sufficient and the maximum dose not exceeded. The exact amount of these important doses may vary according to such factors as the rate of delivery, the density of ionization per unit volume and the susceptibility of the tissue in the irradiated volume.[4]

Radium may be considered the primary method of treatment in carcinoma of the cervix uteri even though most plans of management utilize both external roentgen rays and intracavitary radium implantation, and usually the external radiation is applied first. The simplest method of intracavity therapy is the use of an intracervical tandem. Here the source of radiation is placed in the center of the tumor, and the amount of radiation reaching the periphery is limited by the inverse-square law. In order to partially circumvent this basic property of all radiations, improved techniques have been evolved utilizing two major principles or a combination of them. The first may be described as the multiple source principle, by which as many weak sources of radium as possible are placed throughout the available space.

* From The Los Angeles Tumor Institute. Presented at the Thirty-second Annual Meeting, American Radium Society, New York, N. Y., May 25–26, 1950.

Each source contributes to the sum of the irradiated field to achieve uniformity, but the local reaction immediately adjacent to each is comparatively small. The second principle is in the opposite direction in that the field of radiation is improved by increasing the source-surface distance. There are limitations to the extent to which these principles may be applied, which are

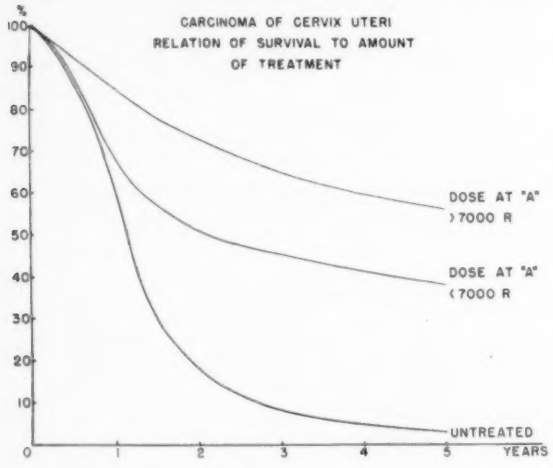

FIG. 1

imposed by the available geography of the cervix and the vaginal fornices and by the nature of the radiations themselves.[5]

Comparison among several examples of intracavity radium applications may be made upon a theoretical basis. If one assumes that there be a maximum dose which will cause undesirable necrosis and that this necrosis must be kept within a finite volume of tissue, the allowable exposure by each applicator may be so limited. Further, it has been demonstrated that there is a vital area in the parametrium, designed as the paracervical triangle. Doses in this area, though not of the necrosing intensity, may not exceed certain finite levels in order to avoid unfavorable effects. If these limitations are excepted, the maximum exposures allowable for each method may be calculated and the resultant fields of radiation in the parametrium may be compared. Such calculations indicate that there is a slight widening of the area lateral to the cervix which may be effectively irradiated as the techniques of radium implantation are improved. However, none of the methods can deliver a theoretically effective dose of radiation to the area adjacent to the pelvic wall save the Neary applicator, which was designed to accomplish this, but it is limited by overdosage at another point (namely, injury to loops of bowel which may lie in the pelvis).

Such an analysis shows us that radium alone may not be sufficient for the treatment of carcinoma of the uterine cervix because the volume subjected to theoretically sufficient dosages is limited. The field of lymphatic spread remains essentially untouched. This problem is attacked by the use of external roentgen rays. The usual methods of treatment utilize radiations of sufficiently high quality to allow for penetration to depth and are given in divided doses to allow for recovery of the skin. It is only with the betatron that tissues deeper than the entrance portal may receive higher doses, but with qualities of 5 mm. Cu or higher the amount of radiation allowable may be limited by reactions in the bowel or bladder. Usually the fields chosen are those which will cover the areas of possible lymphatic spread. Large, centrally placed anterior and posterior fields may result in overdosage to the bladder and rectum, so usually smaller fields placed laterally in the pelvis are used. It is wise to refrain from crossfiring the cervix by angulation of the beams, as this may result in overdosage in the center of the pelvis if external roentgen rays are combined with intrauterine radium. In order to avoid such limitations there has been a tendency in recent years to employ more exacting techniques, which use small multiple portals directed carefully at the parametria. Higher doses may be delivered and areas which may later receive high dosage from the radium may be avoided. Precision therapy of this type should allow for effective dosage to the fields of extension and lymphatic spread.[7] In line with these principles, there has been a philosophy

that external roentgen rays are most important in advanced disease, as radium may be in early lesions. In order to utilize the effectiveness of the roentgen radiation to its maximum and not exceed the tolerance of the application of each. Not only should vital areas be protected from over-treatment, but also irradiation of unnecessarily large volumes of normal tissue should be avoided.

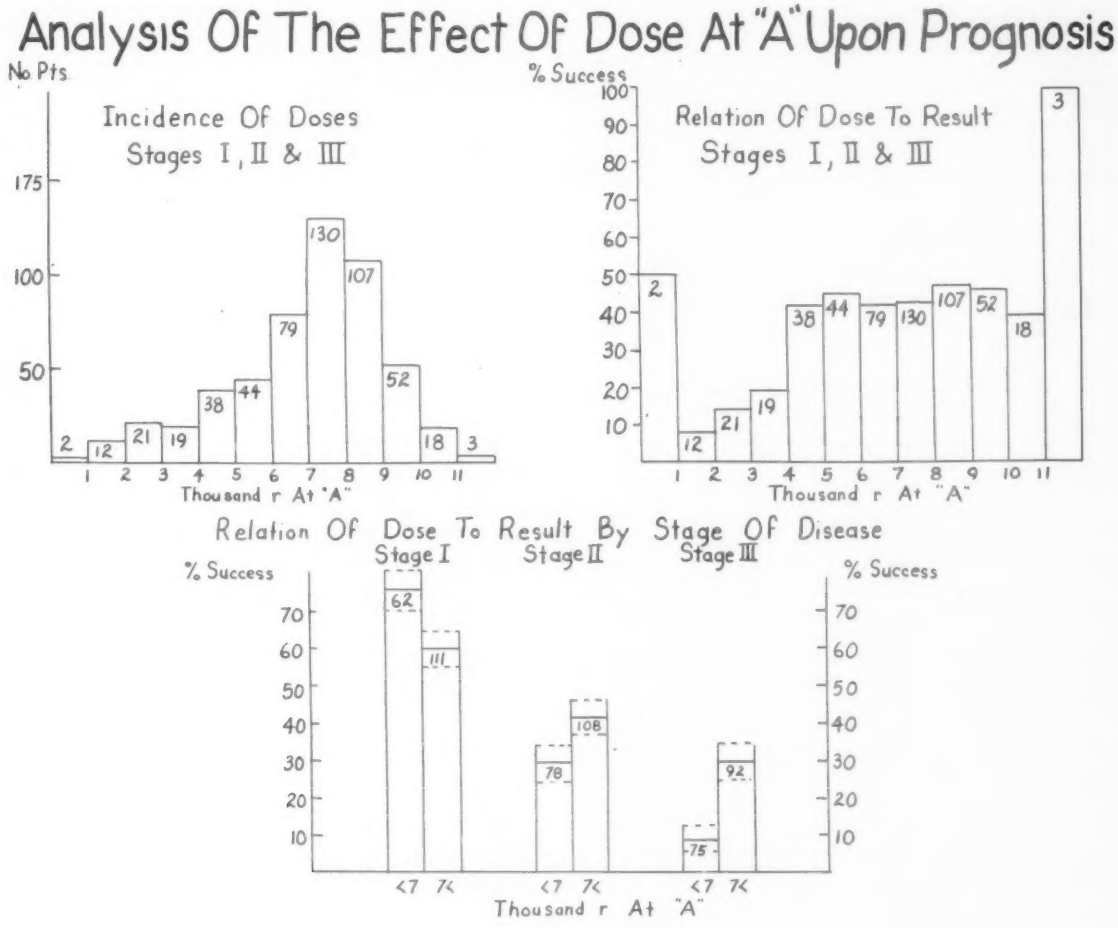
Analysis Of The Effect Of Dose At "A" Upon Prognosis
No Pts
Incidence Of Doses
Stages I, II & III
Thousand r At "A"
% Success
Relation Of Dose To Result
Stages I, II & III
Thousand r At "A"
Relation Of Dose To Result By Stage Of Disease
Stage I
Stage II
Stage III
% Success
Thousand r At "A"

FIG. 2

the tissues immediately adjacent to the cervix, this type of therapy has been combined with transvaginal roentgen therapy.[3] With the latter technique, the energy delivered will be highest at the cervix and vaginal mucosa some distance away from the paracervical triangle.

Theoretically, then, we may describe the best course in planning therapy for an individual patient as one which will utilize the available means of treatment to their optimum limits. If more than one modality is to be used, some care should be taken in

PART II

Justification for such attention to details of dosage distribution can be made only on the basis of clinical results. Recently a statistical survey was made upon the records of 560 patients treated at the Los Angeles Tumor Institute between the years 1933 and 1944. The results of this study will be reported in detail by Dr. William E. Costolow at a later date.[2] However, part of these data may be used to illustrate the relationships between the dose delivered and clinical response.

As far as the effect of the amount of treatment in general is concerned, we may compare the per cent survival curve for patients treated with doses above a theoretically effective level at point "A" in the pelvis with that for patients treated with lower doses. The former indicates definitely better results. Both curves are greatly superior to one taken from the literature to indicate the course of 67 untreated patients with carcinoma of the uterine cervix.[6] However, further investigation of this group of patients brought out other interesting facts.

CARCINOMA OF CERVIX UTERI
ANALYSIS OF STAGE I FAILURES

	DOSE AT "A" <7000 R	DOSE AT "A" >7000 R
LOCAL RECURRENCE		
EVIDENCE OF PELVIC RECURRENCE ON CLINICAL EXAMINATION OR AUTOPSY	9(15%)	34(31%)
DISTANT METASTASIS		
NO EVIDENCE OF PELVIC DISEASE ON CLINICAL EXAMINATION OR AUTOPSY	3	7
ACUTE INFLAMMATORY REACTION		
DEATH FROM EFFECTS OF TREATMENT BEFORE RECURRENCE	0	2
INSUFFICIENT INFORMATION		
LOST FROM FOLLOW-UP WITH RESIDUAL DISEASE OR NO INFORMATION CONCERNING LOCAL RECURRENCES	3	2

FIG. 3

The effect of the primary treatment was investigated in relation to clinical success, criteria for which excluded all but those patients who survived five years or more without developing evidence of recurrent disease at any time in the follow-up before or after the five-year period. The per cent success rate for the primary treatments seems to increase with an increase in dose delivered at point "A." The percentage of successes is higher in patients with small lesions than with more extensive tumors, as would be expected, but there is a significant improvement in results when higher doses are delivered to advanced lesions. This is not true in early tumors, since the per cent survival rate is significantly less good with high doses.

At the outset this reversal in expected results with Stage I tumors appeared quite strange, so an investigation of the available data was carried out along several lines. The prognostic influence of three biological characteristics was first explored. In brief, it was found that two of these factors (namely, the growth type and the age of the patient) may well exert some prognostic influence, but this influence was thought not to account for the superior results in the Stage I cases when treated with low doses. This was because the individual characteristics were equally divided among the subgroups receiving high and low dosage.

The influence of complications was studied. Here three types of adverse reactions were encountered, which were: irritative phenomena, inflammatory reactions, and fistulae. When the incidence of complications by type was studied, it was found that the irritative phenomena showed a dependence upon dose; there was no definite dependence upon stage of disease; and there was no demonstrable influence upon success or failure of the treatment. It was shown that an increase in the number of complications did not account for the superior results in Stage I patients treated with lower doses.

A third line of reasoning was followed in order to investigate the apparent failures in patients with early lesions subjected to "adequate doses." A condition termed "supralethal effect" has been described not only by excessive tissue destruction in the paracervical triangle, but also by persistent or recurrent tumor in this area. In the analysis, failures by reason of recurrent disease in the pelvis represented 72 per cent of the 60 patients in the Stage I group. These patients presented evidence of recurrent tumor on clinical examination, or showed evidence of disease in the pelvis at the time of death. Of these, 34 were in the high dosage group and 9 were in the low dosage group. These numbers represent 31 per cent of the high dosage group and 15 per cent of the low dosage group respectively. The difference between these percentages is significant at the 5 per cent level, which fact may contribute evidence of deleterious effects of overdosage.

Such an analysis suggests that some clinical failures may be due to environmental changes consequent to the treatments, which allow for activation of the growth processes of early tumors. At least, the theoretical concept of a maximum dose may be borne out in practice.

tients in the entire series who were subjected to low doses to make deductions on the basis of the criteria used in calculating the success rates. To be sure, none of the 29 patients in the Stage III group who were subjected to doses less than 4,000 r at point "A" survived. If one assumes that the

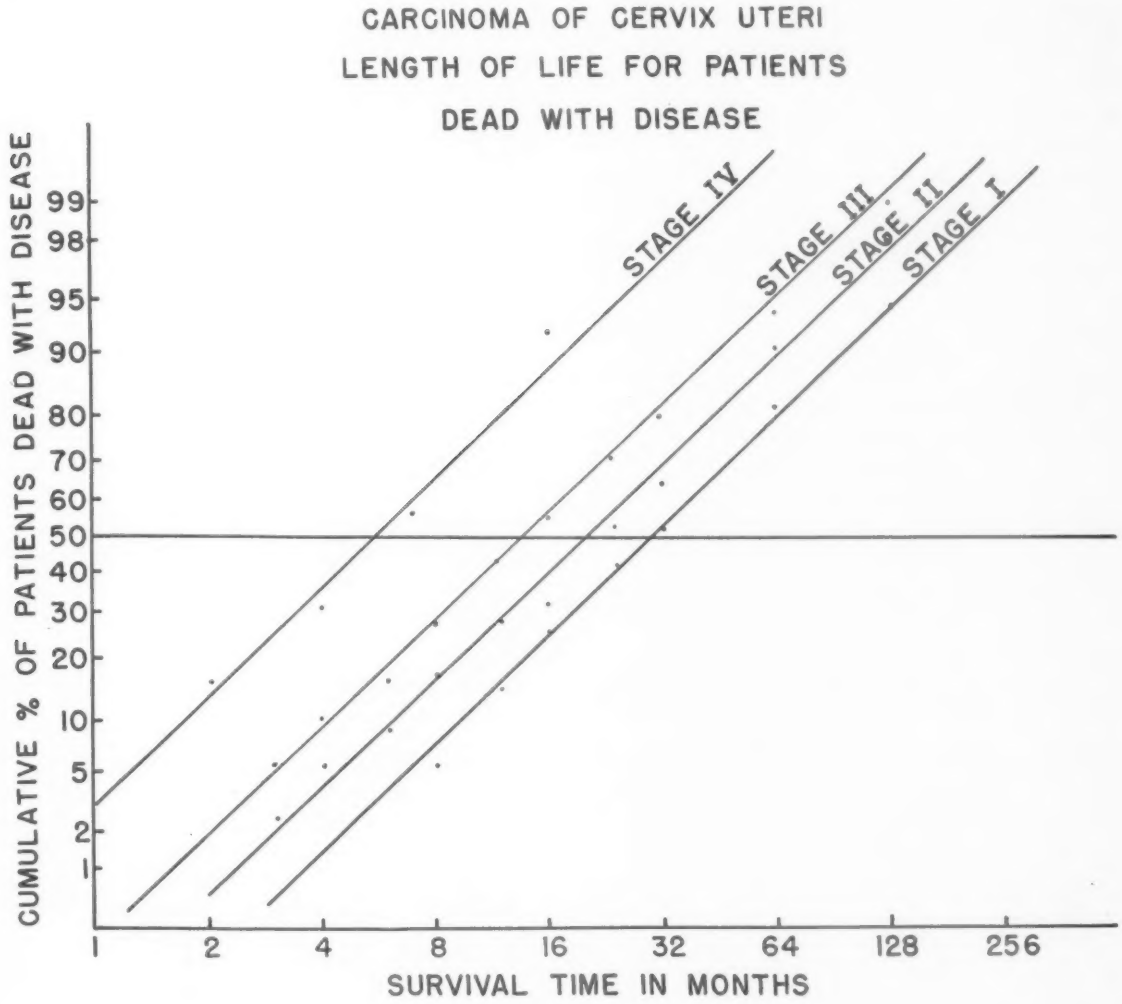

Fig. 4

If overdosage is important, it is natural that its effects be apparent only in relation to early lesions. The effects of underdosage would appear most conspicuously in relation to advanced tumors. However, the role of a theoretical minimum dose is difficult to evaluate from a statistical standpoint. There were not enough pa-

disease had reached this point in all of these patients, the failures may be attributed to underdosage. However, there is a concept which is perhaps the converse of the one previously explored concerning clinical failures in the face of "adequate dosage." This may be stated as the theorem that clinical successes in all patients may not be

due to complete destruction of morphologic evidence of residual cancer. Here it is suggested that environmental changes may be set up which control the activity of the tumor. The effects of underdosage may be apparent in relation to the length of time of such control.

To investigate this theory, it would be impossible to use the successful patients, although we may gain some ideas from the study of the patients known to have died from the disease. We find that the percentage of those patients who will succumb, do so in a normal distribution with the log of time.[1] The period by which 50 per cent of those who died have done so, varies with the stage of disease, so that one-half of the Stage IV patients are dead at six months and one-half of the Stage I patients die by two years and five months.

The influence of the amount of treatment to which these clinical failures were subjected can be seen when one compares the mean length of life for patients treated with high and low dosage. Figure 5 shows these results:

CARCINOMA OF CERVIX UTERI

MEAN LIFE OF PATIENTS WHO DIED WITH DISEASE

DOSE AT "A"	STAGE I	STAGE II	STAGE III	STAGE IV
>7000 R	39 MOS.	35 MOS.	30 MOS.	9 MOS.
<7000 R	36 MOS.	28 MOS.	17 MOS.	8 MOS.

FIG. 5

The results indicate that the degree of palliation which may be achieved is increased by higher doses even in patients who will succumb to the disease. This observation leads us to believe that underdosage plays a part in some clinical failures, and that the theoretical minimum dose is of practical importance.

SUMMARY

This discussion was designed to state some of the principles followed in the technical application of radiation therapy for carcinoma of the uterine cervix. Further, an attempt was made to show some relationship between these theoretical principles and the results of treatment by various correlations between dosage delivered and clinical response. It is hoped that such a demonstration will emphasize the necessity for technical improvement in treatment methods in order to achieve improved results.*

The authors wish to express their appreciation to Mrs. Virginia Hoffman Trask for the follow-up in this study.

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* For discussion see page 722.

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END RESULTS OF RADIATION TREATMENT OF CANCER OF THE CERVIX UTERI*

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IF THE opportunity of participating in this symposium had presented itself a year earlier, I would have expressed my views before this Society with reservation, fearing that my colleagues in the specialty of gynecology might look askance at what I had to say and accuse me of deserting their ranks for the plaudits of the radiotherapist. However, since that time Hoge[1] has published the results of his inquiry sent to the heads of the gynecological departments of the 77 medical schools in this country and Canada. So overwhelming is the opinion of these men, who are charged with the task of instructing future physicians, that I include a table from the original article which shows that but 1.3 per cent of them employ surgery alone in the treatment of Stage I carcinoma of the cervix. So impressive are the results, as depicted in this table, that I have reproduced it here for fear that many have not seen the report.

To add further evidence in favor of radiation treatment of carcinoma of the cervix, we have carefully selected a group of patients, using the same selectivity exercised when one chooses patients for surgery. When this is done, care must be taken in defining the method of selection. In this series, all patients having previous therapy, either surgical or radiation, were excluded, because such therapy alters the behavior of the neoplasm and makes the application of the full course of therapy inadvisable. We also excluded all patients who failed to accept or complete the course of therapy for reasons of their own. If adverse reaction to the therapy necessitated withdrawal of the patient by the medical director, this case is included in the series, because we interpret this as a failure of the treatment. Table II shows that from May 1, 1933, when 800 kv. roentgen radiation first became available, until 1945, there were 499 patients with cancer of the cervix admitted to the Mercy Hospital Institute of Radiation Therapy; 311 of these are considered as recurrent according to our definition as stated. The remaining 188 cases are considered as primary, because they fulfill our definition for the selection of a patient for this category.

TABLE I

SUMMARY BY HOGE[1] OF THE USUAL TREATMENT OF CARCINOMA OF THE CERVIX ACCORDING TO STAGES* BY 77 MEDICAL SCHOOLS OF THE UNITED STATES AND CANADA, 1948

Usual Method Used	Percentage of Schools			
	Stage I	Stage II	Stage III	Stage IV
Irradiation alone	66†	90.9†	100†	100†
Combination alone	19.5	9.1	0	0
Surgery alone	1.3	0	0	0
Multiple methods	13			

* League of Nations definitions.

† Exceptions were made as follows: Stage I to irradiation alone, 13 schools; Stage II to irradiation alone, 8 schools; Stage II to combination alone, 4 schools; Stage III to irradiation alone, 4 schools; Stage IV to irradiation alone, 3 schools.

TABLE II

CARCINOMA OF THE CERVIX

Mercy Hospital Institute of Radiation Therapy
1933–1945

Recurrent cases	311
Primary cases	188
Total	499

TREATMENT

All patients suffering with cancer of the

* Presented at the Thirty-second Annual Meeting, American Radium Society, New York, N. Y., May 25–26, 1950.

cervix are treated with a combination of radium and roentgen therapy, because we believe either agent is inadequate, if used alone, in any situation other than a lesion entirely confined to the cervix. Inasmuch as we can never be certain that this is so, it is considered a dangerous practice to rely on radium alone. If the disease is clinically recognizable at the first examination, the pelvis is carefully evaluated by rectovaginal examination, under sodium pentothal anesthesia, and the clinical grouping of the extent of the disease recorded. The cervical canal is then carefully probed and dilated so that curettage can be accomplished and the upward extension of the disease ascertained. Biopsy is performed and, in the Schmitz Group III and IV cases, this is followed by cystoscopic and proctoscopic examination. Radium is next inserted into the cervical canal in tandem in a capsule of adequate length for this particular case. Fifty milligrams of radium element is contained in the capsule which has a thickness of 2 mm. of brass and is covered with 3 mm. of para rubber. The capsule is left in place for thirty hours for a dose of 1,500 milligram hours. This procedure is repeated at weekly intervals for a total dose of 4,500 mg. hr. On the days radium is not in place roentgen therapy is given through numerous ports determined according to our previously described technique.[8] At the completion of this therapy, further radium in the form of plaques, cross bars, ovoids or interstitial irradiation is used as indicated. In most instances, we find this supplemental irradiation unnecessary. If the diagnosis was not easily established, because of minimal disease or the presence of a preclinical carcinoma, therapy is postponed until microscopic proof of the existence of the carcinoma has been obtained. On the other hand, if the disease is extensive and infiltrating the bladder or rectum, roentgen therapy is begun and followed by radium applications planned according to the response of the tumor to the roentgen therapy.

All cases selected for this study were managed according to this routine. Preinvasive carcinomas are not included in this study as we feel that they should be discussed under a separate heading.

CLINICAL GROUPING

The clinical grouping of Henry Schmitz, the founder of our clinic, is preferred, because of reasons already reported.[7] Preinvasive carcinoma is not included in the present groups because it is our opinion that it should be a subgroup receiving special attention. In our study the clinical extent of the disease is the most valuable point for determining the outcome of treatment. For every millimeter that the disease extends away from its mother site the survival rate drops. This demands, therefore, that we seek cancer early in its development and teach its early recognition by considering the first group a very early stage of the disease. Our observations are that the intense campaign being carried on by the teachers of medicine, aided by the American Cancer Society, is succeeding in bringing into our clinics more cases for early diagnosis. Table III, however, shows that but 30 per cent of the cases in this study were what we would consider early stages of the disease.

TABLE III

CLINICAL GROUPING OF CASES STUDIED

Group I	14
Group II	44
Group III	79
Group IV	51
Total	188

MICROSCOPIC GRADING

The grading of tumors according to the method of Broders[1] is given in Table IV. In the early years of this study all records were not complete as to the grade, and therefore 25.5 per cent are so listed. The grading was of little value in the determination of the outcome of the therapy. It was found that the extent of the disease, not the cell type,

was important. Grade 1 tumors, if localized, responded generally as other cell types. In our clinic a tumor is never considered radioresistant until its behavior, while under treatment, establishes this fact. Weekly biopsy study of the cellular changes, or post-irradiation biopsy taken at the completion of the treatment, gives the most substantial evidence of the response of the tumor. It is by this means that we discover those cases which we feel require most careful watching so that other therapy may be instituted when it has been definitely established that the carcinoma is resistant to radiation therapy. The percentages in Grades 1 to 4 are similar to other studies. However, our incidence of adenocarcinoma is somewhat lower than the 5.4 per cent reported by Martzloff.[5]

TABLE IV

MICROSCOPIC GRADING OF TUMORS

(Broders)

Grade	Total	Percentage
1	5	2.6
2	58	30.8
3	60	31.9
4	11	5.8
Adenocarcinoma	6	3.1
Not graded	48	25.5
Total	188	99.7

RESULTS

Table v tabulates the five year survivals of the cases studied. If we were to include the Groups 1 and 11 cases under Stage 1, League of Nations, which would be permissible, then our survival rate would be 75 per cent for this Stage 1. If one considers the fact that this survival rate is obtained without loss due to the therapy, the end results are more impressive. In Table vi we make a comparison with a similar group of cases previously reported but treated with 200 kv. roentgen radiation and a smaller tumor dose. The radium technique is the same in both series, so improvement in end results must be credited to the improved roentgen irradiation.

TABLE V

1933–1945

Clinical Group	I	II	III	IV	Total
Number admitted	14	44	79	51	188
Survival results	13	31	32	6	82
Percentage	92.8	70.4	40.5	11.5	43.6

COMPLICATIONS

Erythema, epilation, desquamation, enteritis, proctitis and cystitis are results of radiation therapy experienced by all patients. However, complete recovery usually follows within six to eight weeks after termination of treatment. Those patients with persistent damage are, as a rule, suffering with recurrent or persistent disease. These patients are re-irradiated with the same full knowledge of the possible disastrous results, as with the surgeon when he recommends surgery such as cystectomy, bowel resection, etc., in an attempt to control the disease. Some patients, because of their biologic make-up, are more susceptible to irradiation and, therefore develop secondary or permanent damage to tissues in the path of the roentgen-ray or radium beam. In Table vii are listed these complications. The persistent cystitis or recurrent bladder irritability is due to fibrosis and telangiectasia

TABLE VI

COMPARISON OF END RESULTS

Clinical Group	I	II	III	IV	Total	I	II	III	IV	Total
Total number	23	36	100	116	275	14	44	79	51	188
Survivals	21	19	30	7	77	13	31	32	6	82
Percentage	91.3	52.78	30.0	6.04	28.0	92.8	70.4	40.5	11.5	43.62

Diarrhea results from similar changes in the bowel mucosa, and the two organs are as a rule simultaneously involved. The vesicovaginal fistula in all 3 cases was due to disease invasion, and 2 of these patients are living comfortably with their ureters transplanted into the rectosigmoid. Other complications, such as colitis and proctitis, are similar to those producing the diarrhea and could all be classed under one heading. Occasional obstruction results from destruction of the bowel mucosa and resultant fibrosis and constriction. Dermatitis is due to irradiation changes in the skin, and the hemorrhage to secondary slough.

TABLE VII

COMPLICATIONS REPORTED

Cystitis	22
Diarrhea	11
Colitis	6
Dermatitis	4
Vesicovaginal fistula	3
Bowel obstruction	1
Proctitis	3
Hemorrhage	1

DISCUSSION

The 188 cases comprising this report had had no previous therapy, and all were treated as follows: 50 mg. of radium element in tandem filtered by 2 mm. of brass and 3 mm. para rubber for 1,500 mg. hr. every eight days for three applications for a total of 4,500 mg. hr. This administers 7,000 gamma roentgens to area A and 1,540 gamma roentgens to area B. On the days the patient is not receiving radium therapy she receives daily roentgen treatment to one field. The plan for roentgen treatment is as follows: 800 kv., 10 ma., 70 cm. focus-skin distance, filters Pb 1.0 mm., Sn 1.56 mm., Cu 2.62 mm., Al 3 mm., extension chamber 2 mm. of 3 mm. Cu half-value layer; 56 per cent is obtained at 10 cm.; 250 or 300 r is administered daily, and the number of fields are regulated by the measurement of the patient. A total tumor dose of 3,500 to 4,000 r is given. Supportive therapy is given the patient from the start, and hospitalization for the entire time is preferred.

Erroneous interpretation of the publications of Meigs[6] and Brunschwig[2] makes it necessary that we re-evaluate the results of radiation therapy in the treatment of cancer of the cervix and comment on some of our observations. That selection of patients is necessary is evidenced by the fact that surgical series exclude patients with disease beyond certain limits, except in some series where complete pelvic exenteration is performed. It is inaccurate, therefore, to make comparison between such studies and the reports of the radiologically treated series, which include all patients subjected to therapy. The large number of patients (311) excluded from our study is evidence of the large number of cases unsatisfactorily treated before being referred to a center staffed and equipped for the care of cancer. More and more of these failures are due to inadequate surgical methods based on misinterpretation as mentioned. The possession of a scalpel is more dangerous than the possession of a radium tube or roentgen-ray machine as the opportunities for the use of the first mentioned instrument are far greater.

Clinical stage grouping of tumors is a valuable adjunct in the selection of treatment and determining the end result of therapy. Experience increases one's proficiency and, therefore, invites more brilliant results due to more carefully planned treatment. Knowing the pelvis, the lymphatics, blood vessels and ureters is mandatory, whether the treatment is to be surgical or radiation therapy. The radiation physicist has made it possible to calculate the dose obtained in any region of the pelvis, and therapy must be based on such exact principles if it is to succeed. In our method the radium dose at point A is 7,000 gamma roentgens and at point B 1,540 gamma roentgens. The roentgen-ray dose at each of these points is 3,500 r.

Following a complete course of roentgen and radium therapy, as described in our

procedure, further treatment with these agents is not undertaken unless sufficient time has elapsed to justify such a repetition. If the disease persists as a visible lesion, or as evidenced by biopsy, surgical means are utilized as a last resort to eradicate what has proved to be a radioresistant tumor. If healing has taken place and at least six months intervened, further roentgen therapy is attempted, as a number of such cases, 20 per cent according to Calkins,[3] respond to the additional irradiation. The practice of routine extirpation of the uterus following radiation therapy has not appealed to us, because many cases will be lost in this manner. Those with entrapped cells often have so much fibrosis that the disease never reactivates, and breaking down this protection may lead to more rapid recurrence.

SUMMARY

Evidence compiled by Hoge demonstrates that the heads of the departments of gynecology of the medical schools of the United States and Canada prefer radiation therapy over surgery in the treatment of cervical cancer. A review of the cases admitted to the Gynecological Service of the Mercy Hospital Institute of Radiation Therapy shows that from May 1, 1933, to May 1, 1945, there were 499 patients with a diagnosis of cervical carcinoma. Three hundred and eleven of these had been previously treated by surgery or irradiation and were being referred because of recurrence or persistence of disease. As such previously treated patients cannot be managed according to the treatment as planned in our clinic, they were eliminated from this study. The remaining 188, having had no previous treatment, are presented to show the end results of a planned course of radiation therapy. Of these patients, 43.6 per cent are free of evidence of disease after five years. Those cases having immediate recurrence and persistence of disease are sometimes subjected to surgery as a last resort. Thirty-five such surgical procedures were instituted, and they will be reported in a subsequent publication. The complications associated with irradiation of the pelvis are reviewed and are found not to be frequent or severe enough to condemn this method of therapy. The cell type of the disease in no way aided in prognostication. The response of the tumor to therapy and the extension of the disease, however, definitely influenced this prognosis. It is therefore recognized that any marked progress in salvaging the patient suffering from carcinoma of the cervix must be made through early detection of the lesion.

CONCLUSION

One hundred and eighty-eight primary carcinomas of the cervix treated with radium and roentgen radiation are reviewed. The five year cure rate was found to be 43.6 per cent. Factors influencing the response of the tumor to therapy and the indications for surgical intervention are mentioned. There is no evidence that primary surgical treatment holds any advantage over radiation therapy.*

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* For discussion see page 722.

THE POSSIBILITIES OF RADICAL SURGERY IN CANCER OF THE CERVIX UTERI RECURRENT AFTER RADIATION THERAPY*

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THE prognosis for patients with carcinoma of the cervix uteri recurrent or persistent after initial radiation therapy is generally considered to be very bad. A second attempt to control the disease by irradiation, while successful perhaps in isolated instances, is generally regarded to be unsuccessful, and restraint of growth is usually the best that can be envisaged. In the past two and one-half years at the Memorial Hospital a surgical program for these patients has been pursued and whereas sufficient time has not elapsed to evaluate results in terms of the conventional five year survival period, a progress report of this study is herewith presented.

TABLE I

PATIENTS RECEIVING RADICAL HYSTERECTOMY AND LYMPH NODE DISSECTION AFTER FAILURE OF CONTROL OF CARCINOMA OF THE CERVIX BY IRRADIATION*

Patient	Time Interval Between Irradiation and Operation	Result
	Good Results	
G.S.	7 mo.	Living and well 2 yr. 5 mo.
F.F.	8 mo.	Living and well 2 yr. 3 mo.
C.	9 mo.	Living and well 2 yr.
B.V.	1 yr. 4 mo.	Living and well 2 yr.
B.M.	2 yr.	Living and well 2 yr.
I.R.	4 yr.	Living and well 1 yr. 6 mo.
M.T.	4 yr.	Living and well 1 yr.
S.P.	7 mo.	Living and well 9 mo.
R.W.	1 yr. 11 mo.	Living and well 8 mo.
	Poor Results	
E.M.	6 mo.	Has vaginal recurrence 1 yr. 11 mo. postop.
B.S.	1 yr. 7 mo.	Carcinomatosis 1 yr. 3 mo.
B.G.	1 yr. 6 mo.	Carcinomatosis in 10 mo.
F.W.	6 yr.	Died 8 mo.
H.P.	5 yr.	Died 7 mo.
B.L.	2 yr.	1 yr. 3 mo.
N.E.	2 yr.	Lived 1 mo., died hemorrhage
M.O.	7 yr.	Died 1 mo.

* As of May, 1950.

These patients are divided into three groups: (1) recurrent or persistent carcinoma limited to the cervix with or without vaginal, parametrial and pelvic lymph node invasion; (2) the carcinoma has invaded the bladder; (3) the carcinoma has invaded both bladder and rectum.

Radical hysterectomy with pelvic node excision for recurrent or persistent carcinoma of the cervix not involving bladder or rectum. The technique of this extensive procedure which is more radical than the so-called Wertheim operation has been previously described.[1] There are in this group 17 patients (Table 1). Two are relatively recently operated upon, i.e., eight and nine months ago respectively. One is living and well one year after operation and one is living and well one year and six months after operation. Five have survived two years to two years and five months after operation, having received the procedure seven months to two years following the radiation therapy which failed to control the disease. Six patients who received the operation six months to seven years after radiation therapy, survived one month to one year and three months. Thus, excepting the 3 patients who are living and well eight months, nine months and one year respectively after operation, there are 6 patients who are living and well one year and six months (1 patient) to two years and five months following operation.

* From the Memorial Hospital for Cancer and Allied Diseases, New York. Presented at the Thirty-second Annual Meeting, American Radium Society, New York, N. Y., May 25–26, 1950.

With the single exception, the survivors are living at least two years following the operation. Seven patients operated upon six months to seven years following radiation therapy are dead within one year and three months following operation except 1 who is alive with recurrences one year and eleven months. Thus appreciable palliation was achieved in 30 per cent of this limited and selected series. In this connection it may be pointed out that in the studies of Truelsen,[4] based upon 704 patients with recurrent disease, 85 per cent were dead of disease before the expiration of a year after the development of symptoms due to recurrences. Less than 5 per cent survived the second year.

It is also of interest to note that the best results were achieved in the group operated upon an average of thirteen months after radiation therapy and that in the patients who have not survived for appreciable periods, the average period between irradiation and operation was thirty-eight months.

Partial pelvic exenteration. This operation consists of removal of vagina, uterus, adnexae, pelvic lymph nodes and bladder with implantation of the ureters into the colon.[3] The intact rectal colon and anal sphincter apparatus permits of control of excretions. A total of 42 patients have received this procedure of which 29 had carcinoma of the cervix with invasion of the bladder. Among these patients 1 is living and well two years five months, 1 living and well one and one-half years and 1, one year after operation; 3 are living a few weeks to a few months; 1 lived for one year and died suddenly, without necropsy (examination three weeks before death revealed no evidence of disease in the pelvis).

Complete pelvic exenteration, i.e., removal of bladder, vagina, uterus, adnexae and colon is performed when all the pelvic viscera are involved by carcinoma.[2] We have performed 74 such operations. Among these 53 were for carcinoma of the cervix. In this group there are 4 patients living and well two years and eight months; two years and four months; two years and four months, and two years respectively after operation. There are 5 additional patients living and well one year and one month to one year and seven months after operation. The 1 surviving two years and eight months had only extensive radiation necroses of vagina, uterus, bladder and rectum with both vesicovaginal and rectovaginal fistulae. The other patients had extensively growing recurrent carcinoma. The remainder in this group of 53 patients are either dead of recurrences or have survived periods of just several months so that they cannot be definitely evaluated at this time.

The surgical mortality of both the partial and complete pelvic exenteration operations is approximately 23 per cent and this mortality is defined as death within thirty days of the operation regardless of cause. There were no operating room deaths.

DISCUSSION

Sufficient time has not elapsed to express our results in terms of five year survival. However, a preliminary impression has been obtained and that is that radical surgery would appear to have something to offer patients with carcinoma of the cervix that for one reason or another has failed to be controlled by irradiation. Patients with recurrent carcinoma limited to the cervix have been rendered free from clinical evidence of disease for two years or more. Patients with recurrent carcinoma of the cervix invading the bladder or rectum, or both of these structures, may be rendered more comfortable for months following the operation than they seemed to have been prior to operation, and some have lived two or more years following these operations, are free from evidence of disease and having active and enjoyable existences with the ability to return to their normal occupations. In addition, partial or complete pelvic exenteration is indicated in extensive irradiation slough with vesicovaginal and/or rectovaginal

fistulae even though viable carcinoma may not be present.

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DISCUSSION OF PAPERS BY DRS. MEIGS, NOLAN, SCHMITZ, AND BRUNSCHWIG

Dr. William P. Healy, New York, New York. This morning we have listened to an outstanding symposium on the problems of cancer of the cervix uteri. The papers represent the thought and work of specialists of wide experience and carry the stamp of authority. In congratulating the essayists I also would like to compliment the Program Committee which arranged this timely and excellent symposium.

Dr. Nolan's paper discusses some of the principles on which irradiation techniques are based and concerns itself chiefly with the technique of radiation therapy on the basis of dosimetry.

While Dr. Nolan rightly emphasizes that radiation therapy for carcinoma of the uterine cervix was first developed on the basis of empiricism, it has always seemed to me that the trial and error methods of the earlier years accomplished a good job in many respects and especially in identifying the limits of normal tissue tolerance. Of course some of us were very fortunate in the close cooperation that existed between the physicist and the clinician in those early years.

His reference to the paracervical triangle is important.

Dr. Nolan says, and I believe correctly, that radium may be considered the primary treatment for cervical carcinoma but that it alone may not be sufficient because the tissue volume subjected to theoretically sufficient dosages is limited and the field of lymphatic spread remains essentially untouched. It was for these reasons that in the early 1920s we instituted the external use of roentgen rays in an effort to fill in the gaps left by radium.

Dr. Nolan especially insists upon attention to details of dosage distribution in order that vital areas be protected from overtreatment and that irradiation of unnecessarily large volumes of normal tissue should be avoided. His discussion of the effects of overdosage and underdosage raises questions worthy of serious consideration.

Dr. Schmitz has given us a splendid report of his group of 188 primary cervical carcinomas treated by 800 kilovolt roentgen rays and radium. His total salvage of 43 plus per cent of five year cures is most encouraging to those of us who still believe that radiation therapy when adequately and properly administered may be the method of choice for the majority of patients suffering from carcinoma of the cervix.

Dr. Meigs' very able report of 75 patients operated upon by radical hysterectomy and bilateral lymph node dissection is presented in great detail with numerous apt comments by the author throughout the text. He frankly and clearly discusses this important major surgical procedure and the difficulties and complications that tend to accompany it without attempting to minimize them.

Dr. Meigs has demonstrated beyond question that modern surgical technique, improved methods of anesthesia and operating room procedures for the prevention of surgical shock permit the operation to be done in well chosen cases with little or no operative mortality. Nevertheless, it is an operation for the expert specialist and not for the average surgeon who may occasionally see a patient with carcinoma of the cervix.

Some years ago I discussed one of the first or preliminary reports by Dr. Meigs on this subject before the American Gynecological Society. At that time I insisted that we were on the threshold of a new era in surgery,

especially with regard to the operative possibilities in selected cases of carcinoma of the cervix, and strongly urged the gynecologists who had grown rusty in the technique of the Wertheim procedure to again become proficient in it.

It is important to note that Dr. Meigs and his staff at the present time are operating upon more than 50 per cent of the patients coming to their clinic. Does this indicate more early cases favorable for operation or are they extending the operability to include selected Stage III patients? Also, in view of the lower per cent of positive lymph nodes found in the histopathologic Grade 1 and 2 cases have they deemed it desirable, other things being equal, to use this as a guide in choosing Stage III cases for operation?

Dr. Meigs has done radiation therapists a great favor by reporting in detail the presence or absence of residual cervical cancer as determined by histopathological studies after hysterectomy in the patients subjected to preoperative irradiation. The marked variations found in tumor response to different types and doses of radiation again strongly emphasizes what has been observed in a desultory way for years and verifies, as Dr. Nolan said in his paper, the "need for more experimental information concerning the biological processes involved before we can completely evaluate our clinical impressions."

Dr. Meigs' constant and repeated references to the great need of a more exact knowledge regarding the so-called radiation sensitivity or radiation resistance of each tumor, as well as of each individual to her tumor, are most important and would seem to point the way for some extremely helpful and constructive research work.

Regarding the question of whether operative or irradiation methods should prevail in the treatment of patients who have carcinoma of the uterine cervix, I think the time has come for mutual cooperation between the proponents of each procedure. Each method has its distinct advantages and limitations which should honestly and frankly be recognized and stated. Inadequate or excessive irradiation is as bad for the patient as incompetent or bungled surgery. Neither should be attempted except by specialists experienced in their respective fields.

As I see it, surgery and radiation therapy, despite their limitations and drawbacks, are here to stay until something better is developed.

Dr. Brunschwig's report of his experience in dealing with a very difficult clinical and surgical problem is not too encouraging. However, when we realize that, in general, the outlook for the type of patient included in his report is hopeless by any other method, we must agree that in a small number of patients something worth while has been accomplished.

Naturally the best palliative results are obtained in the group of patients operated upon because of local or parametrial recurrent or residual disease following radiation therapy. Whether these patients represented inadequately treated or radiation resistant cases of course we do not know.

However, no doubt it is fair to assume that when they came under Dr. Brunschwig's care in most if not all of them there was pelvic lymph node involvement which we know is usually indicative of associated distant metastases. Under such conditions even the most heroic surgery can accomplish only palliation and for a limited time.

Most of us realize that radiation therapy has a very limited field of usefulness in these recurrent cases but in this group of patients with local or even parametrial recurrences in choosing between a competent radiation therapist and an expert surgeon in 100 such cases I am strongly inclined to doubt that more months of comfortable life will be obtained by operation than by irradiation.

Cancer is a disease in which the primary attack, whether by irradiation or by surgery, must be so planned that the entire disease is eliminated, if possible, at that time.

Dr. H. L. Kottmeier, Radiumhemmet, Stockholm, Sweden. It is for me a very great honor to have the opportunity of being present at this important symposium, and you may all be assured that I appreciate this very much.

As to the question of radiotherapy or surgery in treating cancer of the uterine cervix, we at the Radiumhemmet have the experience that hitherto no sufficient reasons have been presented for advocating primary surgery in cancer of the uterine cervix. Without doubt, surgery in the hands of an experienced and skillful surgeon will yield favorable results in selected cases. However, it is in our opinion a great responsi-

bility to recommend the Wertheim or Schauta operation in cancer of the uterine cervix. We only use surgery in cases of recurrence and in cases of radioresistant growths. In 69 cases in which the patient was operated upon because of a local recurrence, the five year cure rate was 29.1 per cent. In spite of the brilliant result Dr. Meigs has presented at this meeting I venture to say that the results with radiotherapy are at least as good as the best results with surgery in selected cases. Table I shows the five year results of radiotherapy in 1,965 cases of cancer of the uterine cervix treated in 1938–44 at the Radiumhemmet. The relative five year cure rate is 42.0 per cent. You must remember that this statistic includes all cases of carcinoma of the cervix occurring among the population of two-thirds of Sweden. In about 15 per cent of the 1,965 patients, who have received treatment, only palliative treatment has been given. Out of the 1,229 patients in Stage I and II, 750 might have been amenable to surgery. Patients who were older than seventy years or weighed more than 195 pounds and also cases of serious extragenital disease, septicemia, serious pelvic infection and cases in which the growth was fixed to one or both pelvic walls, were excluded from this series. In 67.4 per cent of these selected cases the patient was alive without evidence of the disease five years after radiotherapy had been begun.

It has been stated that some types of cervical cancer should be resistant or unsuitable for irradiation. Adenocarcinoma of the cervix has been considered as radioresistant in particular. Our experience at the Radiumhemmet suggests that there does not exist any special type of cancer which is radioresistant. It may be seen that the results obtained in cases of adenocarcinoma of the cervix are comparable to those obtained in the total of cases of cancer of the uterine cervix treated at the Radiumhemmet (Table II). As adenocarcinoma is often soft in type, infiltration of the parametria may easily escape attention on palpation.

TABLE I

THE RADIUMHEMMET, STOCKHOLM, FIVE YEAR RESULTS OF RADIOTHERAPY IN CANCER OF THE UTERINE CERVIX TREATED 1938–1944. DIVIDED INTO STAGES I–IV ACCORDING TO THE LEAGUE OF NATIONS CLASSIFICATION, 1937

Number of patients examined with a view to treatment	2,040
Number of patients not treated	75
Per cent	3.8

Stage	Number of Patients Treated	Percentage of All Stages	Number of Patients Alive without Evidence of Disease	Relative Cure Rate Per Cent
I	200	10.2	142	71.0
II	1029	52.4	520	50.5
III	580	29.5	145	25.0
IV	156	7.9	18	11.5
I–IV	1965	100.0	825	42.0

All cases are histopathologically verified cancers with invasive growth. All patients traced.

Our results with radiotherapy in cancer of the uterine cervix have improved considerably. I believe that the improvement in the results is largely due to the individualization of the treatment and also to the wider use of roentgen and teleradium treatment. Table III shows the typical treatment according to the Stockholm technique. We give usually 4×400 r, on two anterior and two posterior fields, directed toward the lateral pelvic wall about three weeks after the second radium treatment. However, this typical treatment is only given in selected cases. In outlining a proper course of treatment in a given case, particular attention should be given to factors such as type and spread of the growth, general condition of the patient, extent of the infection, and so forth. In some cases it will be found necessary to

TABLE II

THE RADIUMHEMMET, STOCKHOLM, FIVE YEAR RESULTS OF RADIOTHERAPY IN ADENOCARCINOMA OF THE UTERINE CERVIX TREATED 1938–1944. DIVIDED INTO STAGES I–IV

Stage	Number of Patients Treated	Percentage of All Stages	Number of Patients Alive without Evidence of Disease	Relative Cure Rate Per Cent
I	33 (200)	21.3 (10.2)	22 (142)	66.7 (71.0)
II	80 (1029)	51.6 (52.4)	39 (520)	48.8 (50.5)
III	26 (580)	16.8 (29.5)	6 (145)	23.1 (25.0)
IV	16 (156)	10.3 (7.9)	0 (18)	— (11.5)
I–IV	155 (1965)	100.0 (100.0)	67 (825)	43.2 (42.0)

The figures in parentheses are the corresponding figures of all cases of cancer of the uterine cervix, treated in 1938–1944.

begin treatment with intrauterine radium application; in others, again, the first step would be vaginal radium application. In advanced and infected cases, in particular, we apply roentgen or teleradium treatment before commencing brachyradium treatment. In recent years we have varied the roentgen treatment according to the size of the tumor and the spread of the growth. We feel, however, that too much stress has been laid on the necessity of applying 6,000 r to the pelvic wall in cases in which the growth was fixed to the pelvic wall. Large roentgen doses may cause serious injury, which may unfavorably influence the result. Interstitial irradiation we have only used in selected cases. We have so far had no benefit of implantation of radium needles in the parametrium and of intravaginal roentgen treatment. On the contrary, we have in some cases found complications. Having carried out measurements of the dosage distribution in the pelvis in cases of cervical cancer treated by intracavitary radium according to the Stockholm technique, I have been able to point out that the radium in the top of the vagina has a greater influence than the radium in the uterine cavity on the dosage in the area, where the injury in the rectum is usually situated. On the pelvic wall, on the contrary, the intrauterine radium has at least the same influence on the dose as the vaginal radium. On account of these observations we in many cases have increased the intrauterine dose by 25 to 75 per cent and simultaneously decreased the vaginal dose by 10 to 20 per cent. It is important to have the radium uniformly distributed in the uterine cavity.

The measurements have been carried out on patients suffering from cancer of the uterine cervix with a condenser chamber constructed by Sievert. A bilateral extraperitoneal lymphadenectomy according to Nathanson has been carried out during the course of the intracavitary radium treatment.

TABLE III

THE STOCKHOLM TECHNIQUE IN THE TREATMENT OF CANCER OF THE UTERINE CERVIX

A combined brachyradium and roentgen treatment. Teleradium for metastases of the vulva if necessary.

In typical cases the brachyradium treatment is divided into two coincident intrauterine and vaginal applications with an interval of three weeks. Filter equivalent to 3 mm. Pb.

Intrauterine Application: The length of the applicator and the amount of radium correspond to the length of the uterine cavity. No radium in the lower part of the cervix.

Amount of Radium Element: 53–74 mg.

Vaginal Application: One flat or curved box or two or three cylinders are used in order to cover the vaginal tumor surface and to press the fornices toward the lateral pelvic wall. A tampon to the rectum. No additional filter.

Amount of Radium Element: 60–80 mg.

Irradiation Time: 25–28 hours each treatment.

The patient remains in the hospital for three to four days and is usually able to do some work between and after the treatments.

RADIOCOBALT (CO^{60}) AS A THERAPEUTIC ALTERNATIVE TO RADIUM

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Radioactive Isotopes

DURING the years since artificial radioactive elements were first produced by Curie and Joliot (1934), radioactive isotopes of practically all the naturally occurring elements (and others as well) have been produced by one means or another. These radioactive isotopes differ widely among themselves both in respect to the particles and radiation they emit as a manifestation of their activity and in their half-life periods. The considerable quantities of the various isotopes which it is now possible to produce are a direct result of the development of the cyclotron and, during World War II, of the atomic pile (Smyth, 1945).

The availability of such quantities of a wide range of radioisotopes having a variety of half-life periods and emitting various radiations naturally led those concerned with radiotherapy to consider them from the point of view of possible alternative materials to radium and radon. To this end one is chiefly concerned with those isotopes having the following properties: (1) that they emit hard γ-rays, (2) that they have a considerable half-life period—the longer the better, (3) that they may be produced readily in considerable quantities of adequate specific activity,* and (4) that they have such properties as render them convenient to work and use. From these points of view there are a few radioisotopes, all of which are prepared in the atomic pile, which might be used for radiotherapy. These, in descending order of probable suitability as substitutes for radium (Mitchell, 1946) are, radiocobalt (Co^{60}), radiotantalum (Ta^{182}), radioscandium (Sc^{46}), radioantimony (Sb^{124}), radiobarium (Ba^{140}), radiolanthanum (La^{140}), radiozirconium (Zr^{95}) and radiocolumbium (Cb^{95}).

The reactions whereby these isotopes are prepared in the atomic pile, their half-life periods and the types and energy of the radiations they emit are listed in Table 1 which is based on a similar table given by Mitchell.[8] It is seen that the isotope taken to be the most promising substitute for radium, Co^{60}, has a half-life of 5.3 years and, besides a soft β-radiation, it emits γ-radiation eminently suitable for use in radiotherapy; it emits approximately monochromatic γ-rays of 1.2 mev. mean energy which is very similar to the mean energy of the usual filtered γ-radiation from Ra(B+C). The second choice suggested by Mitchell includes Ta^{182} of half-life ninety-seven days, Sc^{46} of half-life eighty-five days (a relatively rare element) and Sb^{124} of half-life sixty days. All these are produced by the capture of a neutron by the stable isotope in the atomic pile, as indicated in Table 1.

The other radioisotopes listed in group 3 of Table 1 are the products of fission in the pile. They emit radiations which may eventually be used for radiotherapy.

The properties of Co^{60} are such that it is the radioisotope whose therapeutic possibilities as a radium substitute are likely to be most fully explored. Therefore it is upon this isotope that we concentrate our attention in what follows.

Preparation and Ordinary Properties of Cobalt

Metallic cobalt is prepared by the electrolysis of a solution of the sulfate $CoSO_4$ containing ammonium sulfate and ammonia. It is tenacious, silver-white in color,

* Specific activity may be defined as the amount of radioactivity present per gm. of material, i.e., it is a measure of the proportion of the material which is radioactive.

with a white pink tinge. It is readily polished and shows a high luster. It has a specific gravity of 8.8, is magnetic up to 985° C. and melts at 1,490° C. On heating in air, cobalt slowly oxidizes; it dissolves slowly in dilute sulfuric acid and readily in nitric acid.

It is strongly magnetic and so may be manipulated conveniently by means of suitable electromagnets.

Preparation and Properties of Radiocobalt, Co^{60}

As already stated in Table 1, radiocobalt

TABLE I

(Mitchell, 1946)

RADIOACTIVE ISOTOPES FOR USE IN RADIOTHERAPY PRODUCED BY MEANS OF THE ATOMIC PILE (LISTED IN DESCENDING ORDER OF PROBABLE SUITABILITY AS SUBSTITUTES FOR RADIUM)

	Isotopes	Reaction for Production	Type of Radiation	Half-Life Period	Energy of Radiation in mev.		Wavelength of γ-rays in X.U.
					β-particles	γ-rays	
1	Co^{60}	$Co^{59}+n\rightarrow Co^{60}$	β^-, γ	5.3 years	0.31	1.30 1.10	9.5 11.2
2 (a)	Ta^{182}	$Ta^{181}+n\rightarrow Ta^{182}$	β^-, γ	97 days	1.0	<1.6	>7.7
(b)	Sc^{46}	$Sc^{45}+n\rightarrow Sc^{46}$	β^-, γ, K†	85 days	0.26 1.50	1.25	9.9
(c)	Sb^{124}	$Sb^{123}+n\rightarrow Sb^{124}$	β^-, γ	60 days	2.45 0.74	1.82	6.8
3 (a)	Ba^{140} La^{140}	$U^{235}+n\rightarrow Ba^{140}\rightarrow$ $La^{140}+\beta^-$	β^- β^-, γ	12.7 days 140 days	1.20 1.41	— 2.04	— 6.06
(b)	Zr^{95} Cb^{*95}	$U^{235}+n\rightarrow Zr^{95}\rightarrow$ $Cb^{*95}+\beta^-$	β^-, γ	65 days	0.40	0.75	16.5

Cb^{*95} is a metastable state of half-life thirty-three days of the stable isotope Cb^{95}. It comes into transient equilibrium with Zr^{95}. K† = K electron capture.

Elemental cobalt usually obtained is a hard, brittle, highly magnetic metal and proves difficult to machine. For these reasons early reports (Myers, 1948) show that an alloy has been sought which is more workable and will not emit significant amounts of undesirable radiation after bombardment in the pile. An inexpensive alloy (45 per cent Co and 55 per cent Ni) known as "cobanic" has been found to be very satisfactory. It has been obtained in the form of wires in several diameters. It is hard and stiff, though it can be machined fairly readily. A wire of 1 mm. diameter broke only after more than twelve bends at 90° (Myers, 1948). It is a highly inert alloy in which no observable changes were seen on the surface after immersion in (N/10)HCl or (N/10)NaOH for one year.

is prepared in the atomic pile from stable cobalt in accordance with the equation:

$$Co_{27}^{59}+\text{neutron (n)}\rightarrow Co_{27}^{60} \qquad (1)$$

that is, atoms of the stable isotope capture neutrons and become atoms of radiocobalt.

According to Mitchell,[8] "there is no doubt as to the practicability of the manufacture of the necessary quantities of Co^{60} by means of the pile. The Canadian pile could easily produce several hundred curies* of radiocobalt every six months and

* The curie is the unit in which quantities of radioisotopes are usually expressed. As originally defined before artificial radioisotopes were discovered, the curie was that quantity of radon in equilibrium with 1 gram of radium. It happens that 1 curie of radon is such that the number of atoms of it which change per second is 3.7×10^{10}. The term curie is now commonly used for that quantity of any radioisotope which is such that 3.7×10^{10} of its atoms change per second. A millicurie is one-thousandth and a microcurie one-millionth part of a curie.

a specific activity of one curie per gram should be obtained."

Co^{60} may also be prepared in the cyclotron by bombarding targets of Co^{59} with deuterons, Co^{60} being formed and protons being emitted in accordance with:

$$Co^{59}_{27}+d \rightarrow Co^{60}_{27}+P. \qquad (2)$$

In both methods of preparation isomeric radioactive nuclei may be formed with with an average wavelength of 10.2 X.U. This wavelength is so close to that emitted by well filtered radium that dosage problems, etc., for Co^{60} cannot be regarded as very different from those of radium.

The β-radiation may easily be removed by filtration. It is completely absorbed by a thickness of absorber corresponding to 0.09 gm./cm.^{2}, e.g., by a thickness of 0.9 mm. of unit density material or 0.1 mm. of silver.

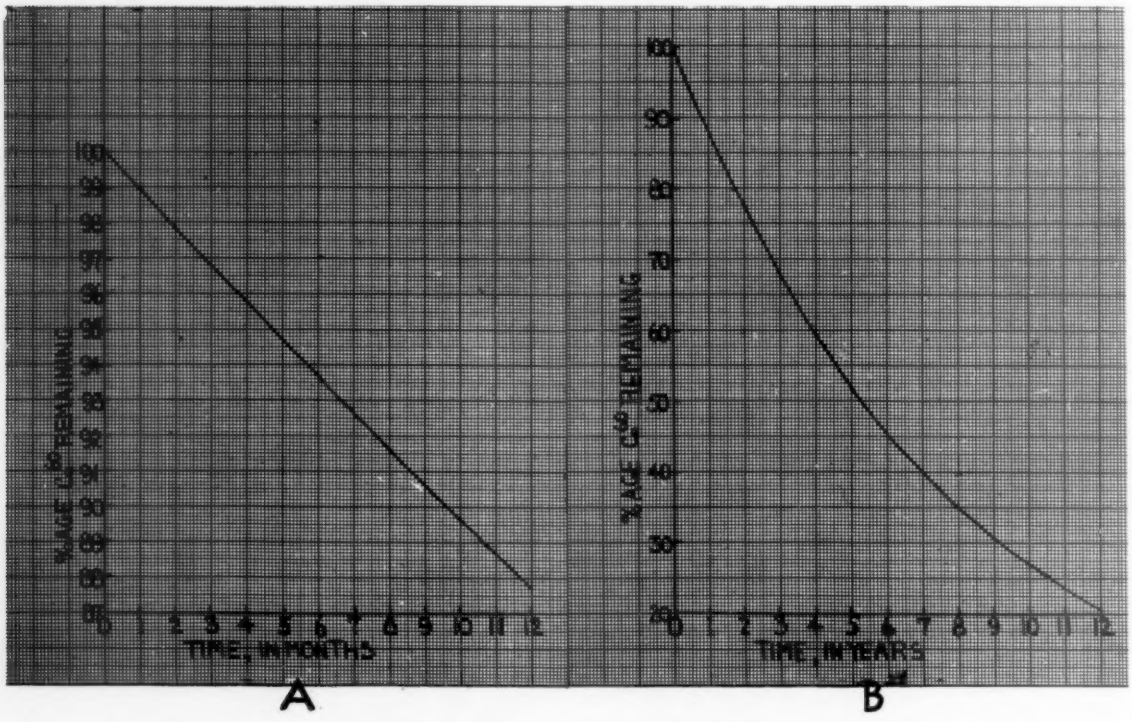

FIG. 1. Decay of Co^{60} (*A*) over period of twelve months, and (*B*) over period of twelve years.

half-lives of 10.7 minutes and 5.3 years; the former is of no importance in therapy. In method (1) only a small part of the Co^{60} is the short-lived isomer and probably most of that which is formed disintegrates to the long-lived isotope (Myers, 1948).

Radiocobalt emits a relatively soft β-radiation of 0.31 mev. energy and a gamma-ray spectrum of two lines corresponding to energies of 1.10 and 1.30 mev. respectively (Deutsch, Elliot and Roberts, 1945); the wavelengths of the gamma rays emitted are thus 11.2 and 9.5 X.U. so that the radiation is practically monochromatic

The half-life period of Co^{60} of importance for therapy is 5.3 years so that its activity decays in accordance with Figure 1 which shows the decay (a) over a period of one year and (b) over a period of twelve years. For practical purposes it is sufficient to assume that at the end of a month the activity is 1.1 per cent less than at the beginning of the month.

At the time of writing* the high specific activity envisaged by Mitchell (1946) has

* A private communication from J. S. Mitchell, 1948.

not yet been realized, but an activity of 158 millicuries per gram has been produced.*

Dosage Rates Provided by Radiocobalt

Using the most recent data, the dosage rate at 1 cm. distance delivered by a point source of 1 mc. of Co^{60} in a platinum envelope 0.5 mm. thick (i.e., 1 Imc. for Co^{60}) is calculated to be 12.2 r per hour. For a bare point source, the corresponding value is 13.0 r/hr. This is for the gamma radiation in each case.

Table II

SOME ABSORPTION DATA FOR THE GAMMA RAYS OF Co^{60} (BASED ON MAYNEORD AND CIPRIANI, 1947)

Material	Density gm./cc.	Mass Absorption Coefficient μ/ρ cm.^{2} per gm.	Absorption Coefficient μ cm.$^{-1}$	Thickness Equivalent to 0.5 mm Platinum mm.
Water	1.0	0.0632	0.0632	
Steel	7.86	0.0538	0.422	1.47
Cobalt	8.80	0.0522*	0.461	1.36
Silver	10.50	0.0519	0.543	1.14
Tungsten alloy	16.50	0.0548*	0.902	0.68
Platinum	21.50	0.0576	1.238	0.50
Gold	19.32	0.0577*	1.113	0.56
Lead	11.37	0.0573	0.651	0.95
Uranium	18.70	0.0638	1.193	0.52

* Interpolated values.

Absorption of the Gamma Rays of Radiocobalt

The absorption of the gamma rays from Co^{60} in a wide range of elements and other substances has been examined very carefully by Mayneord and Cipriani (1947). In Table II is listed some of their data for those materials most likely to need consideration in relation to jackets for Co^{60} sources, absorption in tissues, self-screening and protection. In some cases the data have been interpolated from the values given by Mayneord and Cipriani.

Applications of Co^{60} to Therapy

It is simplest to consider the application of Co^{60} to therapy by discussing each type of therapy in turn. Each type will require its own specific kinds of Co^{60} sources and raise its own individual problems of source activity, dimensions, mounting, screening, etc.

Application to Interstitial Therapy

General Ideas. Following the methods which are well known and have been well tried in interstitial radium therapy, it is natural to make use of linear sources of Co^{60}. In this respect it is first necessary to consider what sort of line sources will provide irradiation conditions similar to those provided by the usual interstitial radium sources and also the best approach to the dosage calculations which will be involved.

In order to relate the dosage calculations for Co^{60} with those for radium, with which we are quite familiar, it seems simplest to work in what might be called "equivalent milligrams" of Co^{60}. Since the dosage rate from a 1 mg. point source of radium element filtered by 0.5 mm. of platinum is 8.4 r/hr. whereas if the radium is replaced by 1 mc. of Co^{60} the corresponding dosage rate is 12.2 r/hr., then 1 mc. of Co^{60} may be regarded as equivalent to $12.2/8.4 = 1.45$ mg. of radium element; i.e., 1.45 mg. are the "equivalent milligrams" of 1 mc. of Co^{60}. Thus, assuming that the

* More recent developments have been such that much higher specific activities are now available.

Co^{60} is used with 0.5 mm. platinum* filter or its equivalent, to a sufficient accuracy for clinical work, all dosage calculations can be made by means of the usual radium dosage charts, the usual milligram hours being read as "equivalent milligram hours."

The line densities of Co^{60} which give the same dosage rates (for the same distance and filter) as those provided by the radium line densities, which experience has shown to be satisfactory, may be calculated by multiplying the radium line density by $8.4/12.2 = 0.691$. Thus, in Table III are listed the radium line densities most commonly used in interstitial therapy along with their equivalent Co^{60} line densities assuming 0.5 mm. Pt filtration.

TABLE III

CORRESPONDING RADIUM AND Co^{60} LINE DENSITIES FOR INTERSTITIAL SOURCES

Radium mg./cm.	Radiocobalt mc./cm.	Diameter of Wire of Co^{60} of Specific Activity 158 mc /gm.
0.33	0.23	0.144 mm.
0.50	0.35	0.178 mm.
0.66	0.46	0.205 mm.
1.0	0.69	0.250 mm.

The bulk, and therefore the diameter, of the Co^{60} line sources required to provide these line densities will obviously depend upon the specific activity of the cobalt or cobalt alloy. In column 3 of Table III we have listed the diameters of cobalt or cobalt alloy wires which provide the Co^{60} line densities set out in the table, assuming the specific activity to be 158 mc./gm. In every case, therefore, a very thin wire will provide the necessary activity. In actual practice, especially when suitable containers have to be provided for the sources, it would probably be preferable to use wire of a fixed diameter and to obtain the various line densities by varying the specific activity. If this is decided upon and the wire has a diameter of 0.234 mm. (i.e., it is No. 34 S.W.G.), the specific activities needed in order to provide the required line densities would be as in Table IV.

TABLE IV

SPECIFIC ACTIVITIES REQUIRED IN Co^{60} WIRE OF NO. 34 S.W.G. (I.E., 0.234 MM. DIAM.) TO PROVIDE THE REQUIRED LINE DENSITIES

Radiocobalt mc./cm.	Specific Activity of Radiocobalt mc./gm.
0.23	68
0.35	91.4
0.46	120
0.69	180

An account of radioactive needles containing Co^{60} has been given by Myers (1948). These were prepared by irradiating in the pile cobalt-nickel alloy containing 55 per cent nickel. They showed uniform linear activity, a wire 3 cm. long and 1 mm. diameter having an activity equivalent to 4.08 mg. of radium, i.e., the linear activity was 0.94 mc. per cm. of Co^{60}. The specific activity thus attained was only 13.4 mc. per gm. of the alloy.

It is preferable, if possible, to use the smaller diameters (of higher specific activity) suggested in Table IV in order to minimize the effects of self-screenage in the radiocobalt and in order to keep the diameters of any containers as small as possible.

Containers and Filters. In deciding upon the kind of containing filter that should be used with Co^{60} wires in interstitial therapy, it is as well to recollect the purposes served by such filters in radium therapy. When the heavy metal filter was first introduced, with very marked improvements in the clinical results, it was considered that its sole function was the elimination of the primary beta radiation. Although this was its main function, it is now realized that the filter also served another purpose.

* If the filter is not 0.5 mm. Pt, the necessary small correction must be made for the actual filter in the same way as is done in ordinary radium practice. There is also the possibility of a small correction to allow for self-absorption of the gamma rays in the cobalt itself but, in general, as is seen later, the cobalt sources are so thin that this is negligible.

The thickness of the container provides a small distance between the actual radiation source and the tissues in contact with the container which prevents the gamma-ray dose to these tissues from becoming excessive (Wilson, 1945).

As we have seen, the primary beta radiation from Co^{60} is quite soft, and is readily absorbed by as little as 0.1 mm. of silver or 0.9 mm. of unity density material. In view of clinical experience with radium, however, and until experience with Co^{60} has been gained, it seems desirable to enclose the wire in containers of wall thickness not less than 0.5 mm. Almost any material might be used, provided it has those other properties which permit it to be buried within tissues; other things being equal, it would be best to use a metal of intermediate atomic number in order to keep secondary beta radiation at a minimum; in some cases thin, hollow, alkathene tubing might be very useful.

Myers (1948) has suggested that screens of nickel 0.1 mm. thick might be used, to be electroplated on to the cobalt before its activation. This would be an intermediate atomic number metal to give a minimum of secondary beta-ray emission, but such a thin filter might lead to dangerously high contact doses, as discussed in the next paragraph.

It has also been suggested that it will be possible to use naked Co^{60} wire with the obvious advantages of easy manipulation, flexibility, etc. This may prove to be so eventually, but if and when it is tried, the possibility of harmful, excessive, contact doses due to the close proximity of the tissues to the wire and due to the added soft beta radiation must be borne in mind.

Dose contours around sources may be calculated by the methods already well established for linear radium sources.[12]

Application to Intracavitary Therapy

In intracavitary radium therapy the chief physical need is for high concentration sources which are either short in length or almost effective point sources, and it is a fact that many physical plans in standard radium practice have to depart considerably from what is most desirable because of the lack of suitable sources. It seems that radiocobalt should prove very valuable in this respect.

Thus, if Co^{60} of 158 mc./gm. specific activity is available, a sphere of it between 3 and 4 mm. in diameter would have an activity equivalent to 50 mg. of radium. Such sources embedded in suitable light atom material, such as one of the synthetic resins, would be admirably suitable for the irradiation of approximately spherical cavities. The self-screening of such sources would only absorb 5 to 10 per cent of the γ-radiation.

In Table v we have listed the line densities of linear radium sources found to be useful in intracavitary radium therapy and the diameters of Co^{60} wires of the above specific activity which give equivalent gamma ray emission. We see that a wire of less than 1 mm. diameter will provide even the greatest required activity. In practice, these could be mounted for intracavitary use within thick containers of light atom material; no other filters would be required to remove the soft β-radiation. In some circumstances, continuous lengths of wire could be distributed in accordance with the usual distribution rules and, even if discrete lengths are used, the inactive gaps which are often so troublesome with radium sources (because of the inactive ends of needles and tubes) should not arise.

Table V

CORRESPONDING RADIUM AND Co^{60} LINE DENSITIES FOR INTRACAVITARY SOURCES

Radium mg./cm.	Radiocobalt mc./cm.	Diameter of Co^{60} wire of specific activity 158 mc./gm.
1.5	1.035	0.306 mm.
2.5	1.73	0.395 mm.
5.0	3.45	0.560 mm.
10.0	6.90	0.790 mm.

Application to Teletherapy

The possibility of many tens of curies of radiocobalt eventually becoming readily available has naturally led to the contemplation of its use as an alternative to radium for gamma-ray teletherapy—units containing up to 50 curies of Co^{60} have been envisaged.* In this connection, two points at least need special consideration: these are (a) the question of self-screenage of the source due to the dimensions that prove necessary for it, and (b) protection of personnel working with the unit.

(a) *Self-Screenage of the Source.* In the design of conventional radium beam units the self-screenage of the salt itself has always been a factor to be considered. The packing of, say, 10 grams of radium element in a source of suitable size for beam therapy has always meant that the source "thickness" must be in the region of 12 mm. or more; such a thickness involves a loss of some 7 to 8 per cent of useful radium (B+C) γ-radiation due to absorption in the salt alone. Although, if a sufficiently high specific activity of Co^{60} can be achieved, the required thickness of the source may be much less, one must still consider that the relatively large absorption coefficient of the cobalt γ-rays in cobalt (see Table II) may still lead to considerable self-screening.

The thickness that a Co^{60} beam source will need to be will depend, of course, upon the available specific activity and the area that the source may take. Conforming with the design of existing radium beam units one may envisage the source as having a diameter of 4 cm. It is then interesting to calculate the volume and thickness of a 50 curie source of Co^{60}, first assuming that the specific activity is 158 mc./gm. (as is available already), and secondly, assuming 1 curie/gm. as may be available eventually. The results are listed in Table VI.

It is apparent at once that the self-screenage of Co^{60} sources for beam therapy is a factor that should be considered. The simplest way of doing this, since it avoids allowances for oblique filtration, etc., is to consider the intensity at a distance d cm. from a cylindrical Co^{60} source of thickness T and radius a where d is very much greater than T and a (see Fig. 2).

The intensity I_P due to disc of thickness

$$dt \simeq \frac{\pi a^2 \rho \cdot dt}{d^2} \cdot e^{-\mu t}$$

so that I_P due to whole cylinder

$$= \frac{\pi a^2 \rho}{d^2} \int_0^T e^{-\mu t} \cdot dt$$

$$= \frac{\pi a^2 \rho}{d^2 \mu} \left[1 - e^{-\mu T} \right] \qquad (1)$$

μ is the absorption coefficient of Co^{60} gamma rays in cobalt (0.461 cm.$^{-1}$). If no self-absorption occurred, the intensity I_P would be

$$\frac{\pi a^2 T \rho}{d^2} \qquad (2)$$

so that with absorption the percentage of the total radiation that is transmitted is:

$$\frac{1 - e^{-\mu T}}{\mu T} \times 100 \qquad (3)$$

The expression (3) thus shows that the percentage of useful radiation which is transmitted from the Co^{60} source varies with the thickness of the source, as shown in the graph of Figure 3. It is seen that the 50 curie source listed in Table VI, of thickness 2.88 cm., would effectively behave only as a $50 \times 55.2/100 = 27.6$ curie source. The

TABLE VI

VOLUME AND THICKNESS OF Co^{60} BEAM SOURCE THE DIAMETER OF WHICH IS ASSUMED TO BE 4 CM.

Specific Activity	Volume of 50 Curie Source	Thickness of 50 Curie Source. Assumed to be 4 cm. diameter
158 mc./gm.	36.0 cc.	2.88 cm.
1 curie/gm.	5.69 cc.	0.443 cm.

* Since this was written plans have so advanced that units containing more than 2,000 curies have been envisaged with corresponding increases in specific activities.

thinner, 50 curie source of 1 curie/gm. specific activity and 0.443 cm. thickness would effectively behave as a $50 \times 90.6/100 = 45.3$ curie source. It is apparent that, if useful radiation is not to be needlessly wasted, it is highly desirable that the beam sources have the maximum possible specific activity.

In actual practice the distance, *d*, for a 50 curie source, would probably be in the region of 20 to 30 cm. It is easily possible to make a similar kind of calculation for

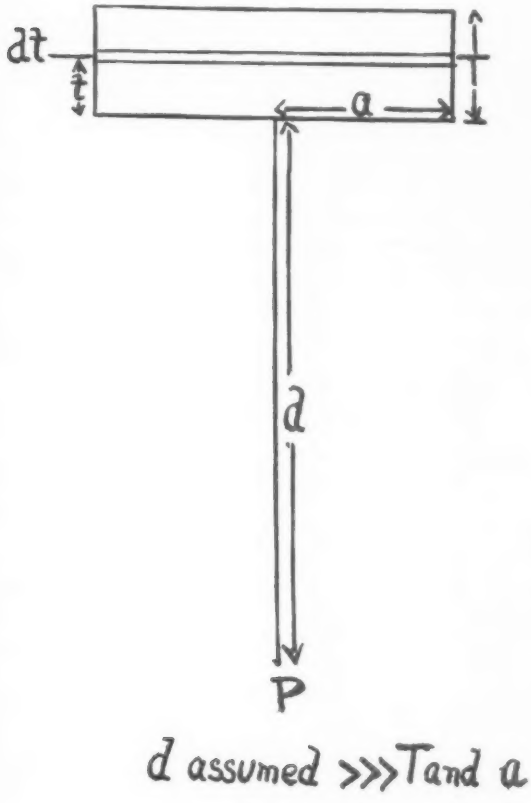

Fig. 2

such conditions and, if this is done, for the range of source thickness in which we are interested, the results are only very slightly different. For the very considerable source thicknesses, the amount of radiation absorbed is somewhat greater.

(b) *Protection of Personnel Working with Co^{60} Beam Units—Practicable Content of Beam Units.* The protection of personnel working with radiocobalt beam units and the practicable cobalt content of such units are necessarily different aspects of the same problem. It is most profitable to consider the problem in terms of existing experience with radium beam units of the most recent type of construction. These units are of the

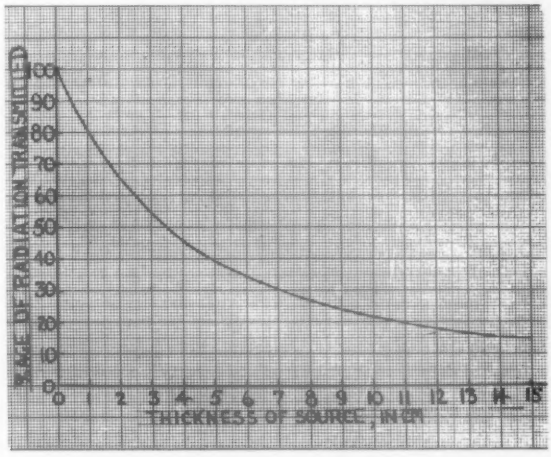

Fig. 3. Showing how the transmitted radiation from a Co^{60} source (after allowing for self-absorption) depends upon its thickness. Results are based on the assumption that the point receiving the radiation is at a large distance from the source.

kind built by Messrs. Bryant and Symons & Co. of Tottenham, London (Grimmett, 1937; Lederman, Clarkson and Mayneord, 1944; Spiers, 1948; Wilson, 1948), which incorporate pneumatic introduction and withdrawal of the radium to and from the unit and, in the most recent models, a protecting cylinder around the radium and nozzles for defining the beam which are constructed of uranium metal. The remaining protection, especially at the back of the unit, is provided chiefly by lead. In earlier models of this unit those parts now made of uranium were made of tungsten alloy (Grimmett and Read, 1935; McLennan and Smithells, 1935).

In order to consider the problem, it is thus necessary to consider the relative transmissions through lead, tungsten alloy and uranium of the γ-rays from Ra(B+C) and from radiocobalt for considerable thicknesses of these metals. Some of the necessary data for this purpose has been

published (Mayneord and Cipriani, 1947; Grimmett and Read, 1935) and some other data are the result of unpublished calculations by F. W. Spiers; they are collected in Table VII below.

Measurements of the stray radiation around a 10 gm. radium unit (Spiers, 1948; Wilson, 1948) in which the protecting cylinder and nozzles are of uranium showed that behind the unit (the region occupied by the working personnel) a dosage rate of 10^{-5} r/sec. is received at a distance of about 1 meter from the unit and at a little over 2 meters' distance the dosage rate is 10^{-6} r/sec. The protection in this direction is provided by about 10 cm. thickness of lead. From Table VII it is seen that the transmission of radiocobalt γ-rays by this thickness of lead is about one-half of that for Ra(B+C) γ-rays. Thus it should be possible to introduce 20 "equivalent grams"* of Co^{60} into the unit and still obtain the same protection in this direction. In view of the fact that the treatment room is usually so large that personnel are more than 4 meters distant from the rear of the unit, it would seem to be possible, if required, to put as much as 40 equivalent grams of radiocobalt into such a unit and still to obtain sufficient protection for personnel situated behind the unit.

Laterally from the unit, where the chief screenage is provided by a 3 cm. thick

TABLE VII

TRANSMISSION OF THE γ-RAYS FROM RA(B+C) AND FROM Co^{60} THROUGH LARGE THICKNESSES OF LEAD, TUNGSTEN ALLOY (16.5 GM./CC.) AND URANIUM (18.7 GM./CC.)

Radium (B+C) γ-rays

Thickness of shield in cm.	1	2	3	4	5	6	7	8	10
Percentage of transmission for lead (μ=0.58 cm. for 2 cm. and more*)	51.0 42.2	31.4	17.6	9.8	5.5	3.0	1.73	1.01	0.30
Percentage transmission* for tungsten alloy (μ=0.87 cm.$^{-1}$ for 2 cm. and more)‡	40.0 37.0	17.6 16.4	7.35 7.6	3.0 3.7	1.29 1.8	0.55	0.22		
Percentage transmission for uranium‡	29.0	11.3	4.6	2.0	0.86				

Radiocobalt γ-rays

Thickness of shield in cm.	1	2	3	4	5	6	7	8	10
Percentage transmission of lead (μ=0.651 cm.$^{-1}$; see Table II†)	52.15	27.2	14.2	7.4	3.88	2.0	1.05	0.55	0.15
Percentage transmission of tungsten alloy (μ=0.902 cm.$^{-1}$; see Table II†)	40.6 39.5	16.5 15.6	6.7 6.2	2.7 2.4	1.1 1.0	0.41	0.18	0.07	0.01
Percentage transmission of uranium (μ=1.193 cm.$^{-1}$; see Table II†)	30.39 30.1	9.10 9.10	2.76 2.7	0.85 0.80	0.26 0.25	0.076	0.020		

* Grimmett and Read.[3]
† Mayneord and Cipriani.[6]
‡ Spiers, F. W. Unpublished calculations.

* An "equivalent gram" of Co^{60} may be regarded, in this connection, as that amount of Co^{60} which emits from itself, after self-screening is allowed for, as much γ-radiation as 1 gm. of radium element in equilibrium with its products.

shield of uranium metal, the protection is such that with 10 gm. of radium in the unit, a dosage rate of 10^{-5} r/sec. is received at a distance from the unit of 2 to 2.2 meters (Spiers, 1948; Wilson, 1948). If it is arranged that personnel cannot approach the loaded unit more closely than, say, 3 meters laterally, then taking into account the absorption of Co^{60} γ-rays in uranium metal (Table VII) and the self-screenage of the source itself, it would seem that sufficient protection should also be provided laterally by the existing units of this type for sources of radiocobalt of up to 40 equivalent grams.

In practice, with such large γ-ray sources, it is certain that one would wish to utilize much larger source-skin distances. This circumstance will probably necessitate larger, and therefore heavier, nozzles and this, in turn, would involve modifications to the units in order to maintain the counterbalances which are essential for smooth and easy rotation of the unit.*

Advantages of Radiocobalt over Radium for γ-ray Therapy

Once an atomic pile is available for the production of Co^{60} as one item among many others, the cost of producing Co^{60} will presumably be very much smaller than that for the preparation of an "equivalent" amount of radium. When a Co^{60} source has been prepared, the costs for its mounting and maintenance should be negligible when compared with similar items for a radium source; this is chiefly because Co^{60} has no radioactive gas associated with it (as radium has radon) and, once a cobalt source has been made uniformly radioactive, it will remain uniform and not tend to become "distorted" as is often the case with radium needles.

Radiocobalt offers very readily the possibility of much greater flexibility and accuracy in the physical planning of treatments than is possible with the usual radium needles and tubes of fixed line density and construction. Thus it should be possible (1) to use distributions of radioactive material which in many cases approximate the ideal requirements more closely than the usual radium sources permit, (2) to easily construct radiocobalt needles of non-uniform loading so that the need for "crossed-ends" in an implant is eliminated and so obtain a better dose distribution in those cases where "crossed-ends" are impracticable, and (3) it should be possible with Co^{60} needles, to reduce the inactive ends to lengths which are not so inconvenient as are those of standard radium needles.

On some occasions, because of the lower intrinsic value of the Co^{60} as compared with radium, it might be possible to treat with Co^{60} as out-patients, some who would otherwise have to come into hospital.

Possible Disadvantages of Co^{60} as Compared with Radium

In many cases it would be possible (theoretically at least) to carry out all the handling required in the construction of Co^{60} sources before they are activated. In practice, however, this would mean that the facilities for a pile would need to be at the disposal of the designer of the sources—not a very likely state of affairs. It is highly probable, therefore, that the advantages of increased therapeutic flexibility which Co^{60} has to offer will in practice only be realized at the expense of either increased exposure to existing personnel or exposure to a greater number. It is obvious that increased numbers of personnel will be essential.

Although the half-life of Co^{60} is relatively long, it is still such that certain small allowances must be made for decay of activity at, say, monthly intervals. This would lead to additional office recording and eventually, after a few years, some sources would no longer be therapeutically useful. Those sources, however, which are of considerable activity initially, in order that they may be useful for work requiring

* In the more recent considerations of very large units of 1,000 or 2,000 curies, focal skin distances of the order of 1 meter are envisaged; under these conditions a very large container may be used for continual housing of the source and the problem is of a very different kind.

such activity, will pass through a stage when their lower residual activity makes them suitable for another type of work. In this way the overall life of such sources may prove to be considerable.

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INDIVIDUALIZED INTERSTITIAL IRRADIATION OF CANCER OF THE UTERINE CERVIX USING COBALT 60 IN NEEDLES, INSERTED THROUGH A LUCITE TEMPLATE*

A PROGRESS REPORT

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INTRODUCTION

THE advantages of tumor irradiation which is homogeneous to the area of neoplasm yet which does not produce heavy irradiation in the surrounding tissue is well understood. The advantage of interstitial irradiation with good dosage control is not widely accepted in this country but the method has gained many adherents in England,[19] and Australia,[5,6] as well as some clinics in the United States.[1,2,3,18,20,22,25]

We have been impressed by the frequency with which complications and unfavorable results, due either to irradiation reactions or extension of tumors which were apparently suitable for radiation therapy, could be explained upon physical measurement to result from the existence of local areas receiving under- or over-irradiation. The problems of biological radioresistance and synergistic application of chemotherapeutic agents[24] defy accurate evaluation unless dosage can be uniform, reproducible, adequate within the tumor, and not damaging to supporting and functioning tissues outside the tumor area. For the immediate future ionizing radiation appears to be the most promising agent for selective control of cancer which cannot be extirpated.

From the above considerations it was decided to investigate radioactive cobalt as an adjunct for radiation therapy. This decision was chiefly governed by the thought that it should be possible to have always available a method which could be accurately adapted to the individual needs of the patients, rather than to have the treatment pattern limited by the available fixed sizes and lengths of radioactive sources.

After preliminary investigations[17] a suitable alloy of cobalt and nickel*** was chosen. Cylinders of cobanic 1 mm. diameter and 1 cm. long were irradiated in the Nuclear Reactor at Oak Ridge for one month. The activity was found to be 1.12 milliroentgens per hour at 1 meter (mrhm) which is approximately equivalent to the gamma ionization from 1.34 mg. of radium element in equilibrium with its decay products and filtered with 0.5 mm. Pt.[17] Even for radium, milligram hours is misleading terminology[15] and must be used with extreme care in individual applications. When referring to Co^{60} such terminology is not practical due to the differences between Co^{60} and radium in quality of radiation emitted.[4,7,8,9,10,11,16] At this clinic the mrhm has been adopted as the unit of intensity of Co^{60} sources.

Animal experiments indicated that the

*** "Cobanic" wire, an alloy of 45 per cent cobalt and 55 per cent nickel, was furnished by the Wilbur B. Driver Company, Newark, N. J.

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From The Departments of Radiology** and Obstetrics and Gynecology,† and The Julius F. Stone Fellowship in Biophysical Research, Department of Medicine.‡

reactions were about two weeks delayed and of an intensity suggesting a biological effect comparable to radium as anticipated for the gamma photons involved. Stainless steel and monel metal tubing* of sufficient thickness for convenient manipulation is greater than theoretically required to completely absorb the 0.32 mev. beta component of radiation. Erythema dose studies are still under way and will be reported later, but sufficient work was done to assure us that the roentgen dosage calculated by physical measurements in this laboratory could be safely substituted for accepted radium dosages in clinical problems.

Suitable spontaneous animal tumors are not common and the problems in large animals are sufficiently different from human tumors as regards the lymphatic drainage, thickness of skin, and difficulties in keeping the observable superficial tumor implantations in accurate placement to limit the usefulness of data secured for projection to cancer therapy in human beings. For this reason it has appeared more fruitful to us to study selected organ tolerances and tissue reactions of normal structures in large and medium sized animals as a guide for possible human uses. Several such studies have been initiated as new problems have arisen, specifically with reference to the ureters and bladder, as well as the bones and vessels of the pelvis. Small animal experiments have been carried out but they are sharply limited in usefulness because of whole body radiation effects.

Human applications have been confined to those instances where no other method of treatment has been available or where previous treatments have failed. It soon became apparent from treating advanced cancer of the uterine cervix that a distinct advantage would accrue from a wider distribution of irradiation.

* Tubing in various sizes and tempers was supplied by the Superior Tube Company, Norristown, Pa.

SELECTION OF CANCER OF CERVIX UTERI

The need for a clinical confirmation of ideas evolved from physical measurement and developments, as well as animal experiments, led to the choice of cancer of the uterine cervix in late stages for further study. Reasons for this choice were: irradiation is the commonly accepted treatment; numerous late cases are always available; progress of the lesion is readily apparent; the tumors presented individual variations on a standard pattern making individualization of treatment advisable; and prognosis could be adequately assessed from previous experience. A major factor in facilitating the progress of these studies is the joint gynecological and radiological treatment and observation clinic.

Review of treatment in late cases† suggested that dosages were governed by the constitutional tolerances of the patients rather than by tumor dosages desired. This was due to inability to irradiate the lateral parametrium sufficiently, without concomitant irradiation of neighborhood structures.

In studying possibilities for individualization of technique we became interested in the work of Corscaden, Gusberg and Donlan.[3] Theoretically, multiple needle implantation gives the optimum possibility for uniform irradiation of cancer tissues.[4] This method has had extensive use for cervical cancer in various centers in the United States. Freehand implantation of the needles, however, often makes it difficult for the operator to secure a predetermined uniform dosage pattern. We have accordingly investigated the possibilities of guided needles and have developed an individualized applicator based

† Treatment of these cases had become standardized with approximately 2,000 r, air dose, to each of two anterior and posterior pelvic fields delivered in twenty days with factors of from 20 by 20 to 15 by 20 cm. ports, 250 kv. (peak), 15 ma., 50 cm. target skin distance, Thoraeus filter equivalent to 3 mm. Cu half-value layer, followed by irradiation of 5,000 r to each of two 3 cm. or 4 cm. diameter circular ports to the vaginal fornices with factors of 120 kv. (peak), 5 ma., 32 cm. target skin distance, 1 mm. Al filtration in ten days plus from 4,000 milligram hours to 6,000 milligram hours of radium in capsules in the cervical canal and fornices.

on the guided needle principle. With this applicator we have been able to treat cases individually, and to secure accurate needle placement hitherto unrealized.

The ability to place needles in predetermined positions reduces the problem to one of adequate clinical diagnosis of position and extent of tumor in the supporting tissues and to uniform theoretical dosage distribution. This tremendously increases the responsibilities of the clinicians and physicists.

PREOPERATIVE CLINICAL EVALUATION

Only League of Nations Stage III and IV tumors were selected for this study. Prognosis in the selected cases was estimated in tumor conference opinion to be one year or less. Irradiation was begun by external therapy, since it was believed inadvisable to lacerate tissues by multiple needle punctures without first securing irradiation inhibition of the tumor, and without the sealing of lymphatics. The external irradiation also clears up infection and distinguishes inflammatory reaction from tumor invasion.

Upon completion of external irradiation† the patients are carefully examined and accurate measurements are taken of the size and position of the tumor; the presence of cervical os and position of cervical face; the relation and size of uterus and cervix to pelvis, vagina, rectum, and bladder; and the size and location of parametrial tumor masses. The size of the vagina was determined by palpation and by the insertion of a series of graduated gauges resembling the templates to be chosen.

A preliminary urological survey is instituted in all cases. This consists of cystoscopy and excretory urography or retrograde pyelography as indicated. Additional urological studies are carried out where indicated.

Facts secured from the above pelvic examination are confirmed by roentgenographic studies consisting of a combined visualization of the bladder, rectosigmoid, vagina, ureters, and cervical canal. Planar roentgenography is found to be very useful by the physicist in analyzing the multiple variations and relationships of the female pelvis in order to determine precise needle positions desired.

Desired tumor dosage remains somewhat empirical, varying between 6,000 r and 10,000 r in a seven day treatment period. Factors governing this decision are extent of the tumor, rapidity of growth, and amount of previous irradiation.

DESIGN OF APPLICATOR

Following the preoperative clinical evaluation and the decision on the desired dosage to the tumor region, an applicator is prepared for the individual patient.

Fig. 1. Cross section of typical needle showing cobalt 60 cylinders positioned by aluminum spacers. Note blunt point secured by cutting tubing with lineman's pliers. After pointing, the needle is loaded from open butt, following which elbow is bent.

In designing the applicators, the irradiation pattern around a line source[14] is the basis for all calculations. It is believed that other methods will soon be available in the near future which will facilitate rapid dosage pattern determination. Basic assumptions in the calculations are: scatter in tissue approximately equals absorption[12] which permits use of the theoretical pattern around line source in air; the stainless steel tubing of the thicknesses employed (0.005 to 0.010 in.) totally absorbs the beta component of the Co^{60} irradiation,[4] shows little scattering effect due to its atomic number,[21] and absorbs a negligible amount of the gamma component of the irradiation;[12] the half-life of Co^{60} is taken to be

† See footnote, page 738.

5.3 years.[13] Current activity of the radioactive cobanic cylinders is taken from a radioactive decay curve for Co^{60}.

Based on these assumptions and using descriptive geometry to calculate the dosage at given points a "standard" applicator was designed which gave an approximately uniform isodose pattern throughout the desired areas with rapid drop-off in intensity for regions outside the applicator proper. The needle distribution has been modified from the Corscaden ideal pattern,[3] which irradiates the cervix, uterus broad ligaments, and lateral pelvic wall. Individual applicators vary from patient to patient in needle arrangement and strength from this "standard" and the regions of greatest variation are investigated to determine their effects in terms of roentgens. Care is taken to assure positioning which is surgically feasible.

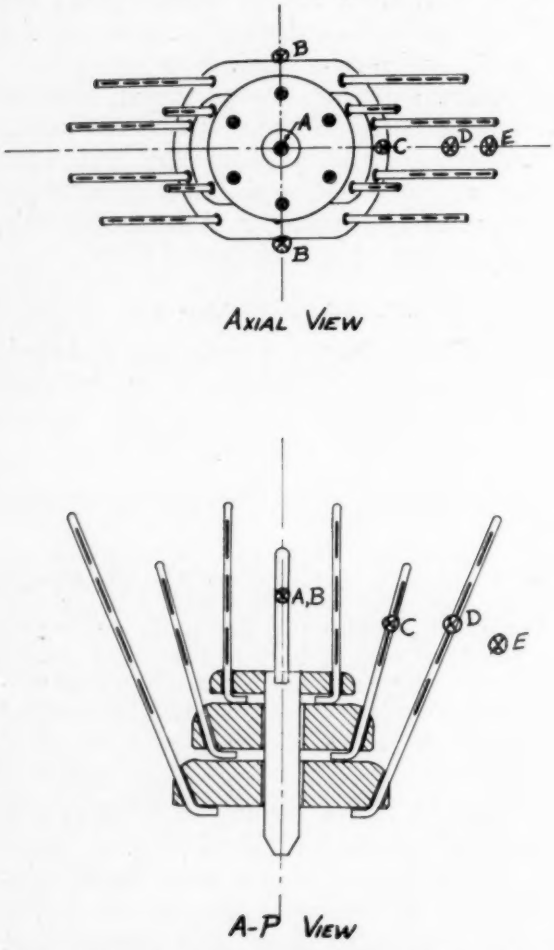

FIG. 2. "Standard" applicator, top view and coronal section showing placement and loading of needles, lucite templates nest over central guide. This is prototype upon which modifications are based. Intensities with this loading of our 1 cm. cylinder sources on March 17, 1949, are:

Point A	Cervical mass	76 r/hr.	5½ days = 10,032
Point B	Bladder or rectum	37 r/hr.	5½ days = 4,884
Point C	Paracervical area	77 r/hr.	5½ days = 10,164
Point D	Lateral pelvic needles	83 r/hr.	5½ days = 10,956
Point E	Lateral pelvic wall	50 r/hr.	5½ days = 6,600

Needles are constructed by inserting cylinders of radioactive cobanic in stainless steel sheathing, and spacing them in the desired positions with aluminum wire or graphite spacers. The lengths of the needles are determined by the mechanical size and placement possibilities of the patient. As a safety precaution, the points are blunted to displace rather than puncture vessels and ureters. The needle butts are bent, which facilitates insertion and prevents migration during period of treatment.[20]

Lucite guides are designed to fit snugly in the vagina, and holes are drilled in them at the proper positions and angles to guide the needles. These guides or templates are made from 0.25 or 0.5 in. lucite sheet. Usually two or three templates are sufficient to assure needle positioning. Additional thicknesses of lucite are frequently necessary to avoid lateral recesses of the bladder with the most lateral needles. Wherever possible, the first plate is positioned by a centrally placed tube, which fits into the cervical canal. All templates are constructed to position automatically relative to each other.

PREOPERATIVE PREPARATION

Patients are admitted for at least twenty-four hours prior to operative insertion. Complete physical and indicated laboratory examinations are made. The patients are placed on low residue diets, sulfasuxidine, and duracillin. Transfusions are given where indicated.

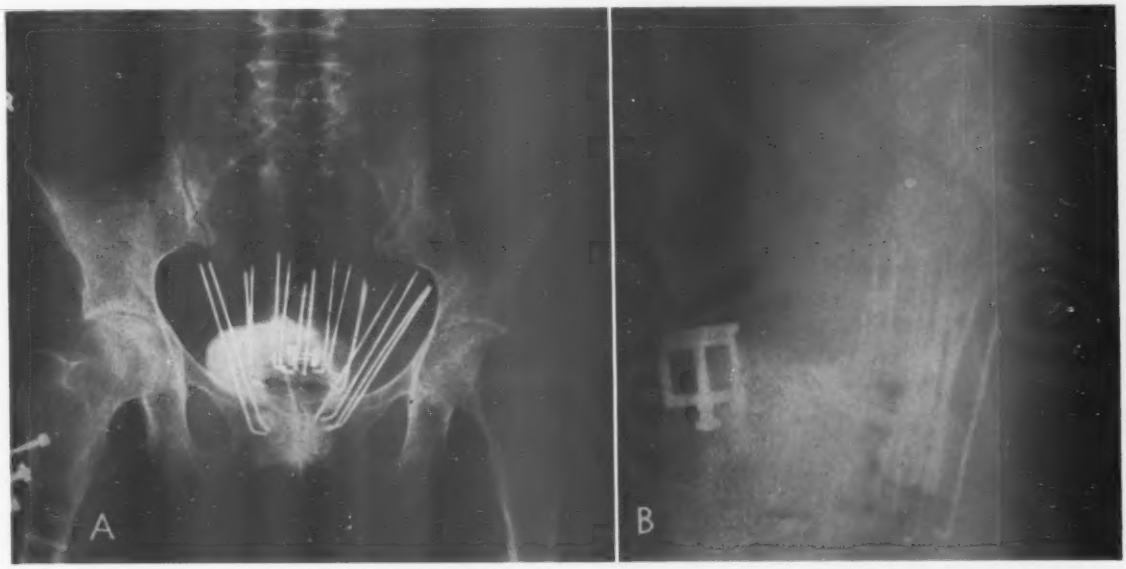

Fig. 3. Anteroposterior (*A*) and lateral (*B*) roentgenograms showing asymmetry of bladder. Bladder extension dorsally on right necessitates asymmetrical pattern. This problem must be recognized by preoperative study. Wide lateral needles enter vaginal wall near introitus.

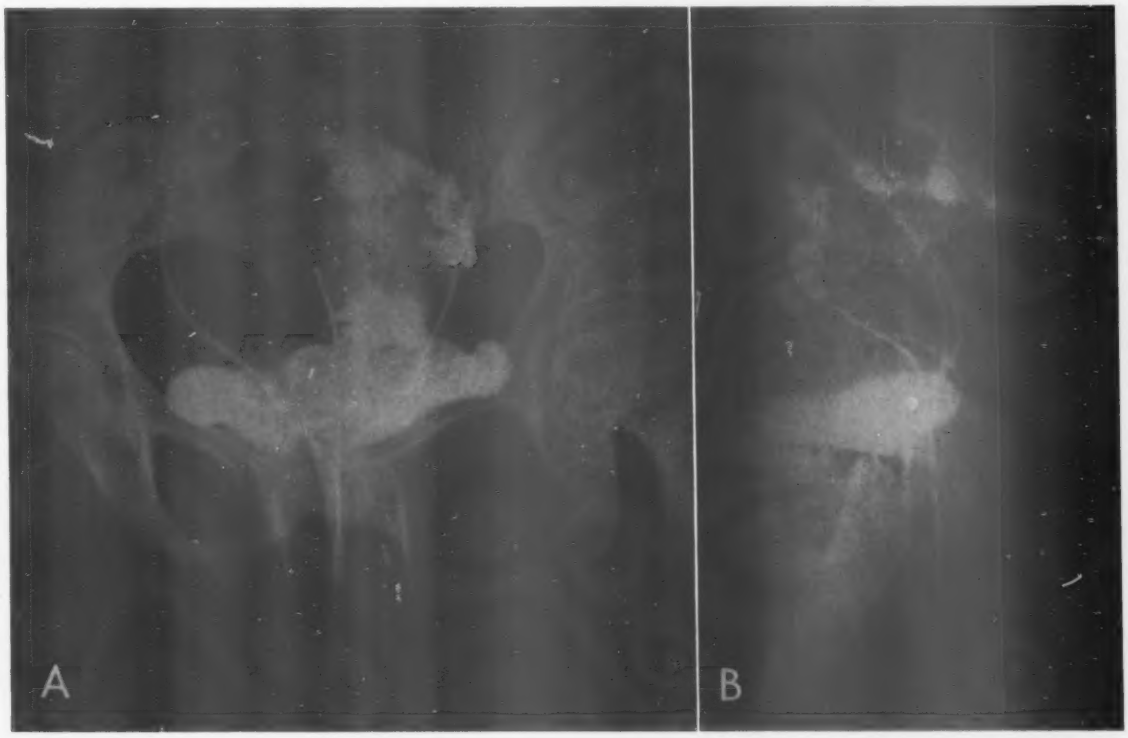

Fig. 4. (*A*) Anteroposterior and (*B*) lateral views of patient showing conventional projections of lateral posterior recesses of bladder, diodrast in bladder, catheters in ureters, barium paste in vagina and barium enema.

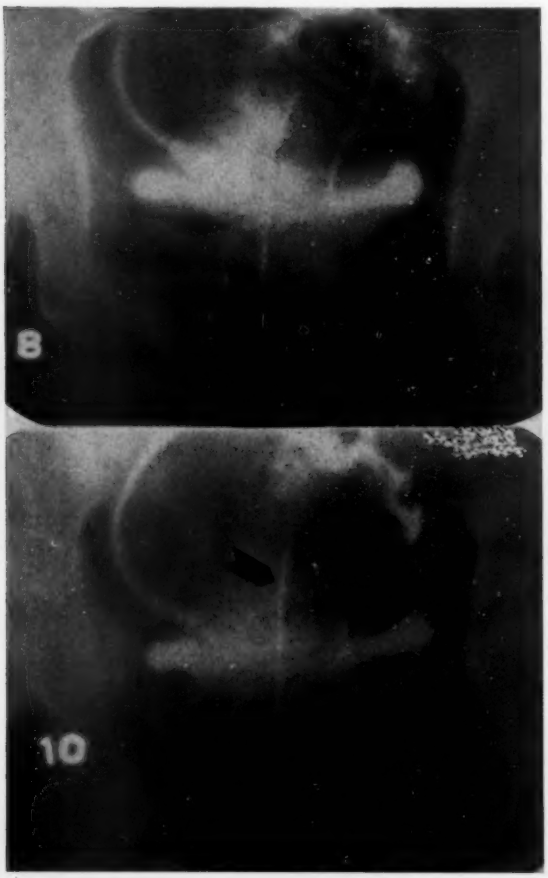

FIG. 4. (*C*) Planar roentgenograms at 8 and 10 cm. from posterior body surface. Arrows show lateral recesses of bladder in sharp forms with ureters at level of parametrium and with portion of cervical probe lying on posterior surface of speculum in vagina. External os of cervix is demonstrated to lie 2 cm. anterior to lateral recesses of bladder.

OPERATIVE INSERTION

The patient is catheterized under anesthesia. A final examination is made. The plates are inserted and the needles individually placed in the predetermined positions. The patient is again catheterized to check for hematuria.

DISCUSSION

In the 9 cases treated to date, no serious complications have been observed. Tumor regression appears to be occurring but sufficient time has not elapsed to consider an evaluation of the method from a therapeutic standpoint.

An edema of the vagina and labia develops at about two weeks after removal of the cobalt and persists for about four weeks. Proctitis and cystitis have not been troublesome. The extrinsic perirectal pseudocarcinomatous induration of Todd[23] has been encountered in one case without

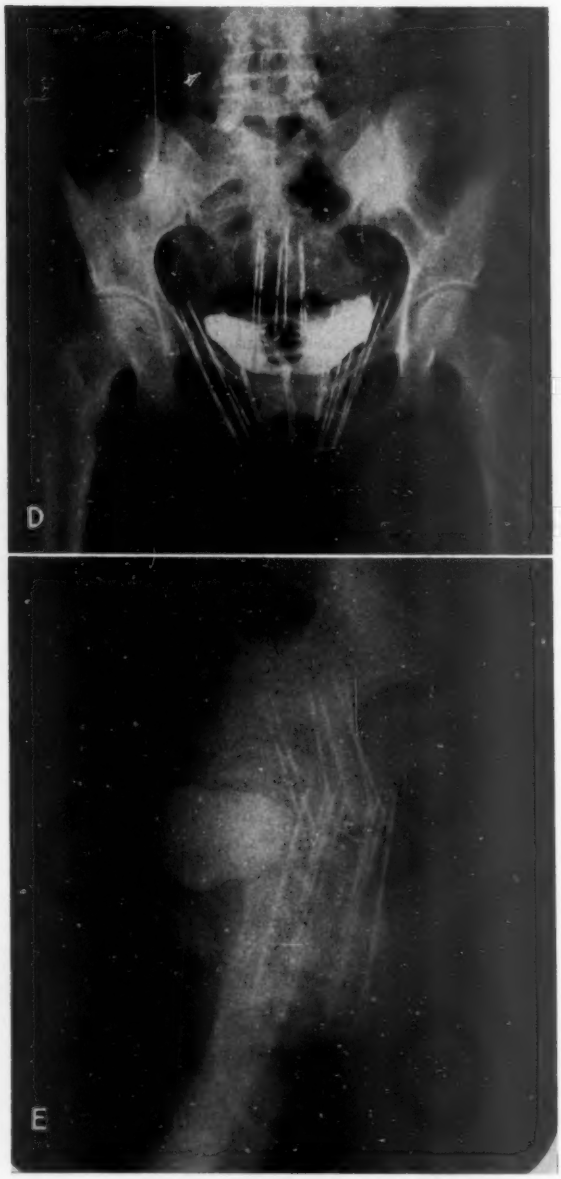

FIG. 4. (*D*) Anteroposterior and (*E*) lateral views of patient after insertion of cobalt 60 showing positions of needles. Note angulation of cervical needles and the fact that no needles transfix the bladder. Wide lateral needles enter the vaginal wall near the introitus.

ulcerations. This is to be expected from the heavy external therapy combined with high interstitial dosage deemed advisable in this case.

Puncture of the bladder is known to have occurred in one case and is suspected to have existed in a second case, based upon the presence of hematuria throughout the treatment period. These cases occurred before the need for adequate roentgen studies of the bladder was appreciated. Cystoscopic follow-up has failed to reveal any significant sequelae, and the patients have had no urologic symptoms. The bladder mucosa of the first case did not reveal the site of puncture after the second week following removal of the needles, and the area could only be identified as a point of bluish submucosal hemorrhage. The presence of bladder puncture in this patient was indicated by hematuria and the needles were withdrawn at the time of

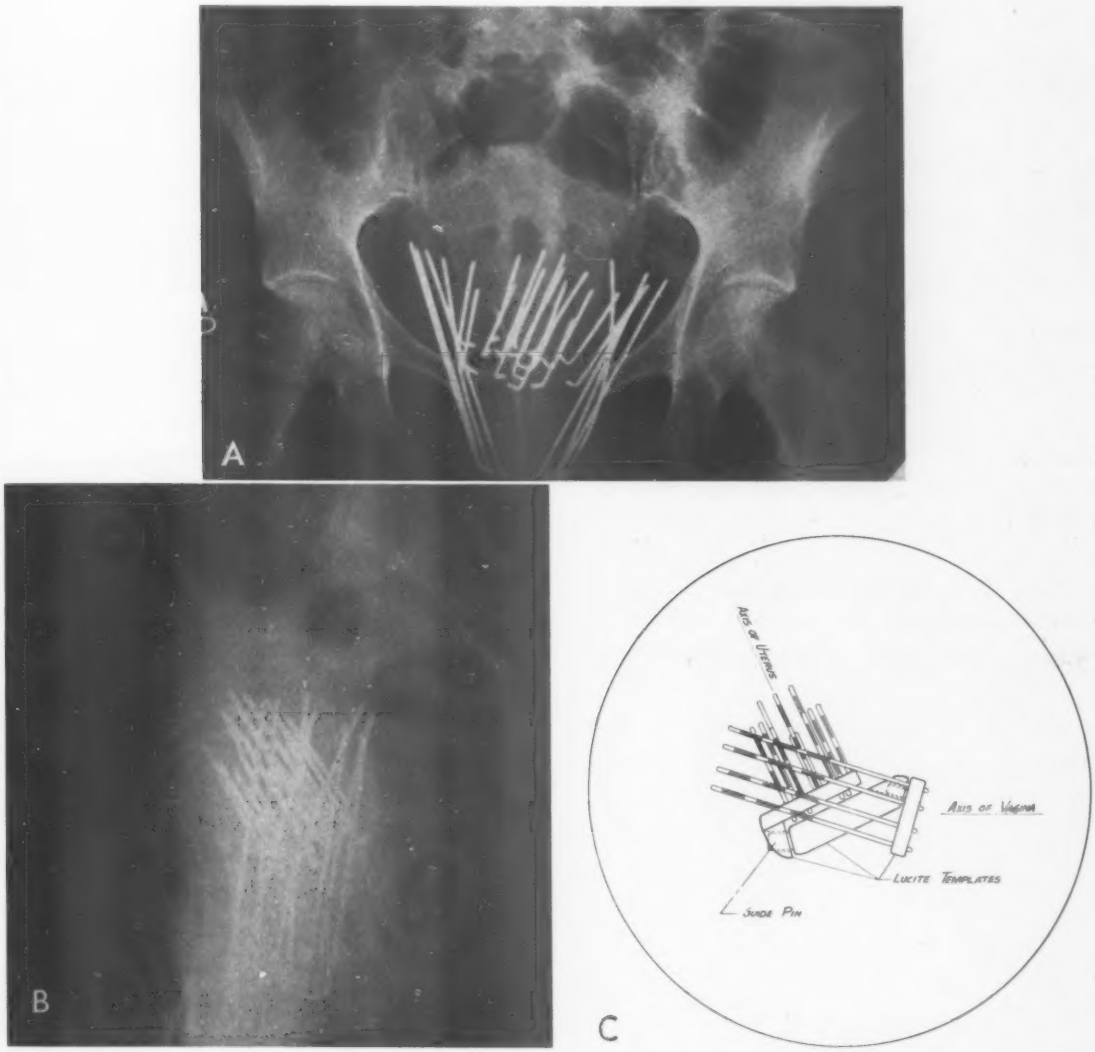

Fig. 5. (*A*) Anteroposterior and (*B*) lateral views showing method of compensating for 60° angulation of uterus to vagina with high rectocele and narrow distal vagina. Rectocele permits entrance of cervical and mid-parametrial needles from innermost plate. (*C*) shows lateral view of applicator as designed. Note the special design of lucite templates to secure needle position.

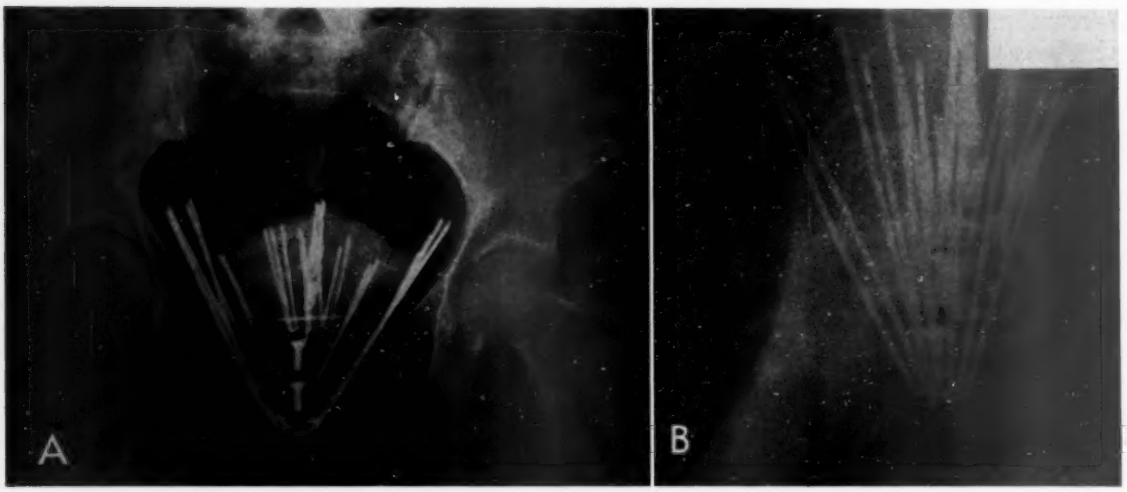

FIG. 6. (*A*) Anteroposterior and (*B*) lateral views show divergence of needles required with small vagina. Contracted vagina resulted in this case from external and intravaginal roentgen therapy six months previously. "Frozen pelvis" with evidence of active tumor growth at time of cobalt 60 insertion.

insertion. The second case, which was not recognized at the time of insertion and which was presumed to have had bladder transfixion and full irradiation, showed similar submucosal discoloration which shortly disappeared.

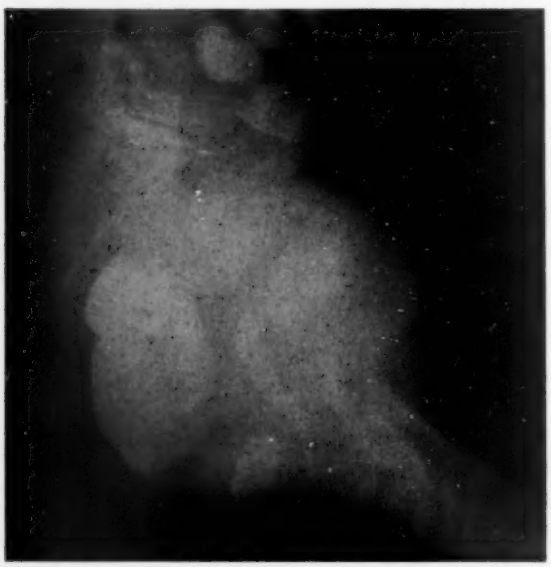

FIG. 7. (*A*) Panhysterectomy for cancer three years previously at another hospital. Recurrence of tumor in vaginal apex and in 5 cm. contiguous nodule dorsal and cephalic to vagina. Pelvic examination and colpocystoproctogram showed bladder anterior and tumor formed 2 cm. thick cap to vaginal apex.

Puncture of the ureters constitutes a theoretical hazard, but we have not recognized such an accident. After careful consideration of the seriousness of the tumor in these advanced cases with the expectancy of early ureteral occlusion by the tumor itself, it has been thought preferable to attempt adequate and uniform irradiation of the tumor in the neighborhood of the ureter. The reactions of the ureter threatened by tumor under irradiation have not been satisfactorily studied. It is hoped by careful analysis of these cases to determine whether ureteral damage occurs and to weigh the various factors contributing to ureteral occlusion.

The patient reaction to this Co^{60} irradiation is similar to that with radium therapy but radiation sickness has been a relatively minor complaint. One febrile reaction of 102.5° F. has been encountered, but in general the patients have been remarkably afebrile. Local discomfort and fullness from the volume of the templates and pack is a frequent complaint but disappears immediately after withdrawal of the apparatus. An iodoform pack is left in the vagina for twenty-four hours after the needles are removed. The patient is discharged after therapy is completed and

continues under observation as an outpatient.

CONCLUSION

There are three aspects to the program of the therapy here outlined which are interrelated but which bear separate consideration. These are: the needle technique for uniformity of radiation distribution; the use of plastic templates for needle guidance and fixation; and the employment of the isotope cobalt 60 as the source of gamma radiation.

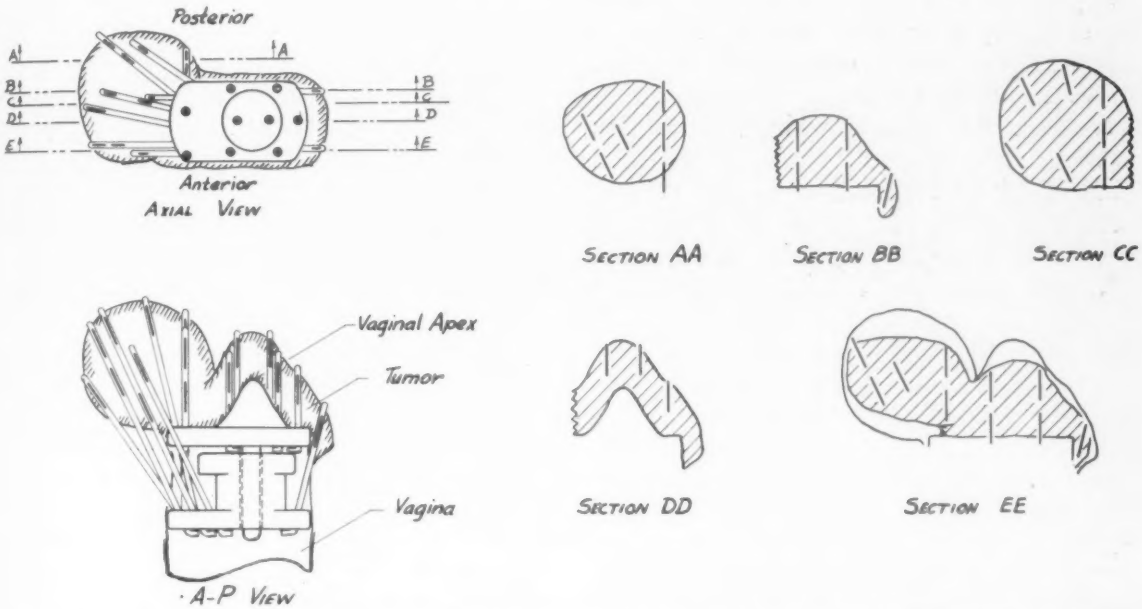

Fig. 7. (*B*) Drawings show needles as projected in tumor and sectional studies showing positioning of cobalt 60 cylinders from which needle design and angulation were derived.

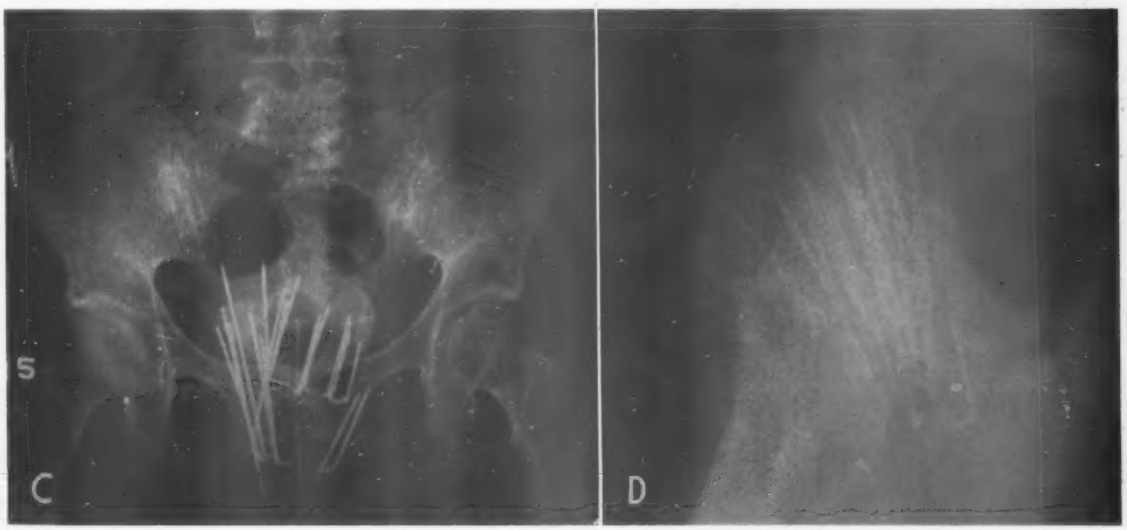

Fig. 7. (*C*) Anteroposterior and (*D*) lateral views showing applicator in place. Note close agreement between the actual and the calculated positions of the needles. Tumor regression was secured.

The authors are cognizant of the dangers inherent in the use of needles in the pelvis for irradiation of cervical cancer. It is

believed, however, that many of these dangers (puncture of viscera and migration of needles during therapy) have been obviated by the use of the template guides and by careful preoperative evaluation of the pelvic status and relationships. On the other hand, the advantages of needles as a source of radiation—uniform distribution of dosage without major "hot spots"—have been retained. Combined with these two mechanical aspects of the proposed plan of treatment, radioactive cobalt has been of great advantage. Not only can the needle distribution be individualized to the patient's needs, but the individual needle strength can be regulated to provide maximum efficiency of therapy. Precision dosage can become individualized precision dosage, and is apparently well tolerated and without unusual or insoluble dangers. Further careful studies seem justified at the present time on the basis of the theoretical and realized potentialities of the method.

Such studies should be directed toward the achievement of a more uniform dosage distribution, through the use of smaller cobalt sources, and toward still more accurate evaluation of tumor distribution, so that the irradiation may be fitted to the individual patient rather than the patient to the irradiation.*

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* The following changes have evolved since the above paper was written:

Cobalt metal in smaller pieces 3 mm. long and 0.5 mm. in diameter is employed.

From 20 to 40 needles are used.

The needle sheathing is made from aluminum tubing which can be dissolved off the cobalt with weak sodium hydroxide.

The pattern includes more of the vagina and, if indicated, irradiates the bladder floor even by transfixion of the bladder.

Blady, J. V. Secondary filters in radium therapy. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 804–818.
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DISCUSSION

Paul Aebersold, Ph.D., Oak Ridge, Tennessee. In discussing this paper, I wish to make clear that I am not qualified to discuss the clinical aspects, but as a physicist, and because of my familiarity with cobalt 60, I was invited to discuss the paper. I trust that others will discuss the clinical features.

The authors do not claim any radically new development over what has already been done by others with radium. They have, however, put together a number of good ideas to improve the precision of the irradiation setup. As Dr. Failla stated this morning, there is very little point in using an artificially produced radioisotope, such as cobalt 60, only as a cheap source of radiation, just as a substitute for radium.

The authors are to be commended for seeking some new applications for cobalt 60. Those mentioned in the paper permit certain unusual achievements along the lines of uniform irradiation and individual tailoring of the setup to the patient. This is possible chiefly because of the low energy of the beta rays from Co^{60}. The average energy of these rays is about 100 kev., so that a very thin layer of stainless steel can be used as an effective absorber. This means that a thin stainless steel hollow needle can be used to contain the active cobalt, thus eliminating the costly expense of platinum needles. With the greatly reduced cost of both the active material and the sheaths, the investigator can make a number of individual applicators without a big over-all investment. The user can thus afford to have several different units patterned for different types of patients. Also, the stainless steel tubing is rigid and is not breakable or malleable. Further, it is cheap enough so that if one wishes to make a new applicator from an old one, the active cobalt can be removed and the old stainless steel sheaths discarded. Besides this, the cobalt can be transferred quite easily from one applicator to another.

The other advantageous feature about stainless steel is its low atomic number. It was pointed out some time ago by radiophysicists that the smaller the atomic number of the material of the needle sheath, the smaller is the amount of secondary radiation set up by the initial gamma radiation. Therefore, fewer secondary electrons are produced in the immediate region around the stainless steel needle than is the case for the platinum needle.

Also cobalt 60 can be used advantageously in loading the long multiple needles. By proper irradiation of a cobalt wire in a reactor you can obtain any specific activity, i.e., any radioactivity per unit length, that you want. For example, we can make radiocobalt wire having a specific activity of 1 mc./cm., 10 mc./cm., or 100 mc./cm. Then by taking different lengths of different specific activity wire and separating them with appropriate aluminum spacers, we can make needles and applicators which will give almost any desired dosage pattern. You can make the ends of the needle applicator "hotter" and the center portion "colder," or vice versa. Another advantage of cobalt 60 is that non-radioactive wire can be machined or bent to any specially desired shape before being activated.

The authors' idea of using templates, of course, is to fix the needles in place so that there will be less chance of hot spots by too close spacing or overlapping of the needles.

Another major point is over-all economy as mentioned before. Cobalt 60 is now available at $50 per curie or fraction of a curie. The second curie also costs $50, but for each additional curie the price is only $5 per curie. This means that 100 curies of Co^{60} would cost about $600 plus handling and shipping costs. Therefore you can get the equivalent of a pound of radium in gamma-ray output for a few thousand dollars. Furthermore there is no limit to the amount of cobalt 60 we can make in terms of curies. Right now we have available small cobalt units about 1 cm. in length and 1 cm. in diameter, which have a specific activity of 1 curie/gm. This is the same specific activity which radium has. In the future we expect to

have cobalt 60 with specific activity of about 3 curies/gm. and this is still not the upper limit.

I would like to point out that the handling of cobalt 60 is quite simple. It can easily be manipulated with a magnet, and because you can tailor make the size and shape of your source before making it radioactive, you can obtain a wide variety of applicators.

Cobalt 60 nevertheless has certain disadvantages which I would like to mention. The first is its comparatively short half-life, 5.3 years. This means that from time to time, corrections for decay must be made. Further, there is little difference between the energy of the gamma radiation from cobalt 60 and the energy of the gamma rays from radium. Consequently, although there might possibly be some advantage in using cobalt 60 because of the uniform energy of its gamma rays, I doubt that this can be demonstrated. Also if you plan to make your own cobalt 60 needles, it is necessary to have the proper shielding and manipulators to do this semi-remotely. You also have to be concerned about possible contamination of your laboratory, but I do not look upon this as an insurmountable difficulty. Possibly the biggest disadvantage to the use of Co^{60} is that it is not commercially available as is radium. At present, it is only available to those institutions which have the facilities for research and clinical care of patients, as well as a trained personnel to use the material. In other words, it is available right now primarily to those clinicians in a position to carry out special measurements and clinical developments rather than routine application.

I would also like to mention that it may be possible to use other reactor-produced radioisotopes in interstitial needles. Of course cobalt 60 is about the best long-lived gamma-ray emitter available, but there are several shorter lived materials which might make good competitors for radon. I am thinking of isotopes such as gold 198 or iodine 131. If anyone is interested in starting a research or clinical program based on the use of new types of applicators, we would be glad to provide advice and assistance.

VOL. 65, NO. 5

INVOLVEMENT OF THE MANUBRIOSTERNAL JOINT IN MARIE-STRÜMPELL DISEASE*

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MARIE-STRÜMPELL disease, or spondylitis rhizomelique, is a form of rheumatoid arthritis involving the sacroiliac joints and spine and occasionally some of the following peripheral joints: shoulders, sternoclavicular joints, costovertebral joints, temporomandibular joints, hips, and symphysis pubis. Knaggs states: "The hips become involved when the disease is active in the lumbar region; the shoulders, sterno-clavicular and temporo-mandibular joints are in danger when the cervical and upper dorsal spine is attacked; and ankylosis of the ribs to the vertebrae probably synchronizes with dorsal mischief."[12] It is doubtful, however, whether any such regional correlation can be made, and it appears rather that these extravertebral joints may be involved in the latter stages of the disease.[4] Very occasionally, Marie-Strümpell disease co-exists with extensive rheumatoid arthritis of multiple peripheral joints, but it usually does not, forming a separate entity. Hare[9] mentions the following major differences between spondylitis rhizomelique and rheumatoid arthritis of peripheral joints:

1. The former is ten times more frequent in males than females, whereas the latter is more common in females.
2. Peripheral joint involvement is infrequent with the former.
3. Pathological changes appear first in the sacroiliac joints in rheumatoid spondylitis.
4. Calcification of the ligaments is always present in the late stages of the former.
5. Relief of pain is obtained by roentgen treatment in Marie-Strümpell disease.

Of the joints which may show pathological changes in spondylitis rhizomelique, no reference to the manubriosternal articulation is found in the medical literature. Involvement of this joint in the peripheral type of rheumatoid arthritis is not mentioned either.[4] Pain and swelling in the region of this articulation are said not to be uncommon in rheumatoid arthritis, but roentgenological changes have not been demonstrated.[10] The xiphoid process was found to be the seat of pain and tenderness in two cases of the peripheral type of rheumatoid arthritis by Barcelo.[1] Pain and tenderness over the costochondral junctions in Marie-Stümpell disease have also been noted.[18] The present report concerns itself with roentgenological changes in the manubriosternal joint in patients with rheumatoid spondylitis.

Abnormalities of this joint were noted in several cases in the lateral dorsal spine films. These changes were studied further by additional examinations of the sternum. Subsequently, all spine surveys made in this department showing the sternum were reviewed. It was felt that some idea of the frequency of involvement of the manubriosternal joint in Marie-Strümpell disease might be obtained from the lateral views of this region, although it was recognized that, for complete study, projections in at least two planes were required. These have been made in the more recent cases.

DEVELOPMENT AND ANATOMY

"The sternum is ossified from two cartilaginous plates, one on either side of the mid-line, which fuse during the second month of foetal life. They may fail to fuse. Ossific centres begin to appear in this cartilage about the sixth month of foetal

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FIG. 1. March 9, 1949. Incomplete obliteration of manubriosternal joint in a twenty-four year old white male. (A) Manubriosternal joint, partially fused anteriorly. (B) Similar process in joint between first and second segments of sternal body.

life. The first is that of the manubrium and this is followed by the nucleus of the second, third and fourth pieces during the interval before birth. A nucleus of the xiphoid appears about the age of three years. These segments appear on the radiograph as distinct bones separated by a narrow strip of cartilage until about puberty. The separate segments of the body fuse with one another at about twenty-eight years of age. The manubrium remains as a separate bone usually throughout life."[3] It may fuse to the body of the sternum in advanced age.[8a] The xiphoid process fuses with the body during middle life.[8a]

The manubriosternal joint is an amphiarthroidal joint with fibrocartilage between the opposing articular margins. A synovial cavity develops in about one-third of the fibrocartilages.[8b] An amphiarthrodial joint "Arises by chondrification of an original membranous plate between separate cartilaginous remnants. It is permanent in character. In the chondrified joint plate, a thin layer adjoining each of the two uniting bones remains hyaline in nature, but the intervening zone of much greater thickness becomes fibrocartilaginous. In some such joints, the center of the fibrocartilaginous plate is modified either by the formation of an irregular slit-like cavity as in the pubic symphysis, or by the presence of a core of

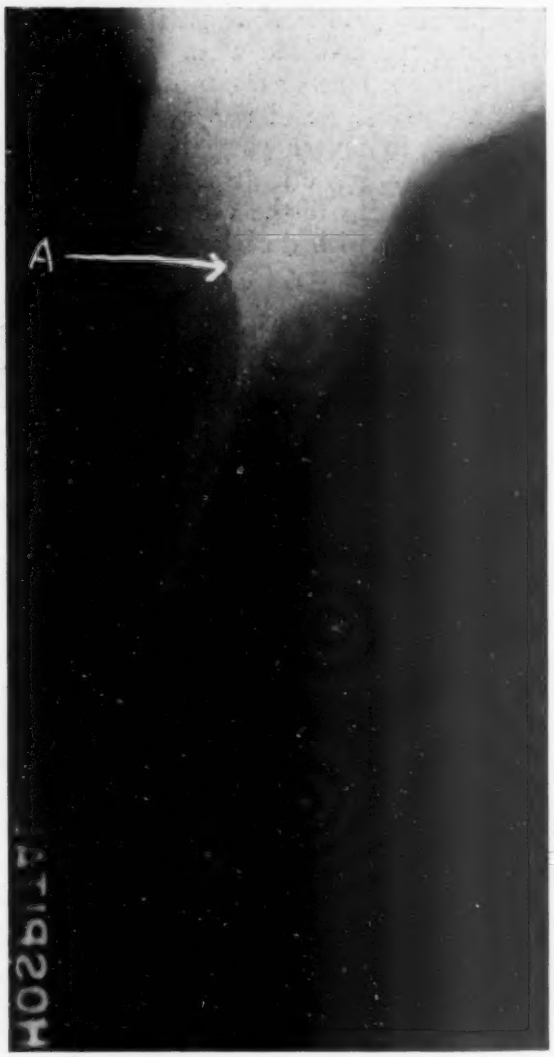

FIG. 2. June 15, 1948. Degenerative changes at manubriosternal articulation. (A) Narrowing of joint space and osteophytes at anterior and posterior margins.

soft pulpy tissue as in the intervertebral disc."[5b] The joints between the segments of the body of the sternum and between the body and the xiphoid process are synchondroses. They are composed of hyaline cartilage until they are obliterated by fusion of adjacent bony segments.

FIG. 3. September 17, 1949. C. A. L., fifty-one year old white male. Onset of rheumatoid spondylitis in 1930. Now has "poker" spine and involvement of symphysis pubis and hips. (A) Erosive changes and incomplete fusion of symphysis pubis.

PHYSIOLOGY

The manubriosternal articulation has a definite function in respiration. During inspiration, the ribs move upward and forward to expand the thorax. "As the first rib is so much shorter than those which succeed it, the upward and forward excursion of its anterior end is less in extent, and the upper border of the sternum is only slightly raised and is carried forward hardly at all. The greater travel—especially in the forward direction—imposed upon the rest of the sternum by the longer ribs causes a bending of the breast bone at the manubriosternal joint."[5c] During expiration, an opposite movement occurs at this joint.

FIG. 4. June 9, 1949. R. W. A., twenty-seven year old white male, with onset of back trouble in 1938. Now has arthritis of dorsal and lumbosacral spine. Articular surfaces of manubriosternal joint show extensive erosion.

PATHOLOGY

In general, rheumatoid arthritis is a disease of synovial joints. The synovia shows fibrous proliferation and round cell infiltration. The proliferating synovial membrane, called the "pannus," gradually extends over the articular cartilages and the latter become eroded and ulcerated. The cartilages are also eroded by granulation tissue which forms in the epiphyses and invades their deep surfaces. Adhesions form between the two layers of pannus and in time the greater part of the entire joint may be obliterated by fibrous ankylosis, in some cases. The tissue uniting the two surfaces of the joint may contain cartilage or osseous material producing bony ankylosis. On the other hand, periarticular inflammatory changes in ligaments and joint capsule may cause softening and absorption of ligaments producing joint luxations and deformities.[2] Inflammatory changes in

the adjacent synovial sheaths of tendons and bursae, fibrous tissue and periosteum may also take place.

Rheumatoid spondylitis begins as an arthritis of the sacroiliac joints, followed by a synovitis of the joints formed by the intervertebral articular facets. The disease ascends the spine and frequently involves the costovertebral articulations. Ankylosis of all affected joints may occur and calcification of the ligaments about the vertebral bodies and posterior arches. In addition, some patients show patchy areas of increased density in the ischia and pubes with roughening of the periosteum and exostosis formation.[12] The symphysis pubis is also sometimes affected. Fairly early, ulcerous defects occur and later bridging of the symphysis.[7] It is of interest in this connection that the posterior or apophyseal joints which are diseased early in rheumatoid spondylitis are true synovial joints.

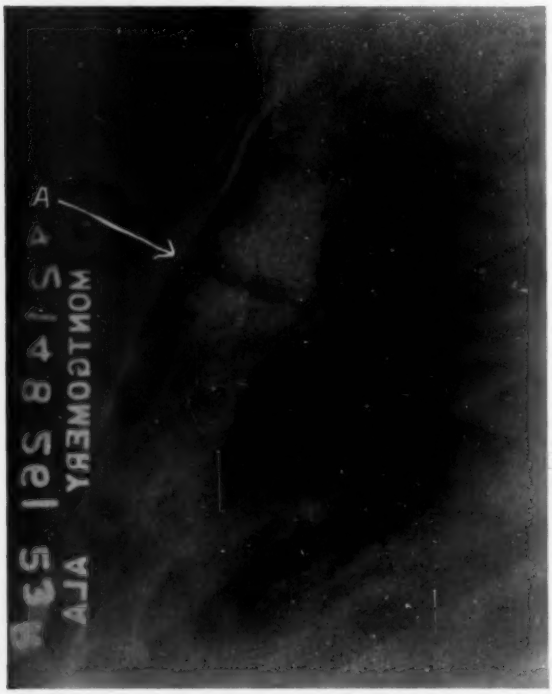

Fig. 5. April 21, 1948. H. J. Z., a fifty-five year old white male, with far advanced rheumatoid spondylitis and rheumatoid arthritis of left knee and shoulder. (A) Irregularity of articular surfaces, increased density of subarticular bone and beginning fusion at anterior margins of joint.

The amphiarthroidal joints between the vertebral bodies, which are not synovial, are not affected except for calcification of the spinal ligaments about them. The ligamentous calcification is said not to be due to intrinsic disease of these joints.[15] The sacroiliac joints are classed by some as amphiarthroidal[8] and by others as diarthroidal.[5] These joints are at least partially diarthroidal, since the anterior and posterior sacroiliac ligaments provide a complete capsular investment lined on the inside with synovial membrane.[5d] The symphysis pubis, on the other hand, is of the amphiarthroidal type, but its fibrocartilage occasionally shows a slit-like synovial cavity.[8c]

RESULTS OF STUDY

A total of 637 spines were examined. Of these, 580 were non-rheumatoid, and 57 were examples of Marie-Strümpell disease in various stages of development. A small number of other cases of far advanced spondylitis rhizomelique could not be included in the study because the sternum was off the lateral film of the dorsal spine due to pronounced kyphosis. Of the 580 non-rheumatoid spines, 32 cases, or 5.5 per cent, showed fusion of the manubriosternal joint. Twenty of these were World War II veterans, whose average age is thirty, and 12 were World War I veterans, whose average age is fifty-five. Five other cases showed a joint between the first and second segments of the body of the sternum in addition to the normal manubriosternal joint. Three other cases showed no joint

Table I

NUMBER OF SPINES EXAMINED

Manubriosternal Joint	Non-rheumatoid		Rheumatoid Spondylitis	
	World War I	World War II	World War I	World War II
Normal	189	349	1	34
Fusion	12	20	8	5
Erosive and productive changes			2	7

between the manubrium and the sternal body, but did show a joint between the first and second segments of the body.

The 57 patients with Marie-Strümpell disease included 13 with complete fusion of the manubriosternal joint. Some of these fused joints appeared to be the end result of pathological change, but most of them could not be differentiated from those noted in non-rheumatoid spines. However, 23 per cent of these joints were fused in spondylitis rhizomelique as opposed to 5.5 per cent in non-rheumatoid spines.

Nine patients, or 15.8 per cent, showed varying degrees of erosion of the margins of the articulation or of the actual joint surfaces, increased density of the adjacent subarticular bone, and evidence of beginning obliteration of the joint. One case showed marked bone proliferation at the anterior and posterior margins of the joint and calcium deposition and beginning bridging at the lateral margins of the articulation.

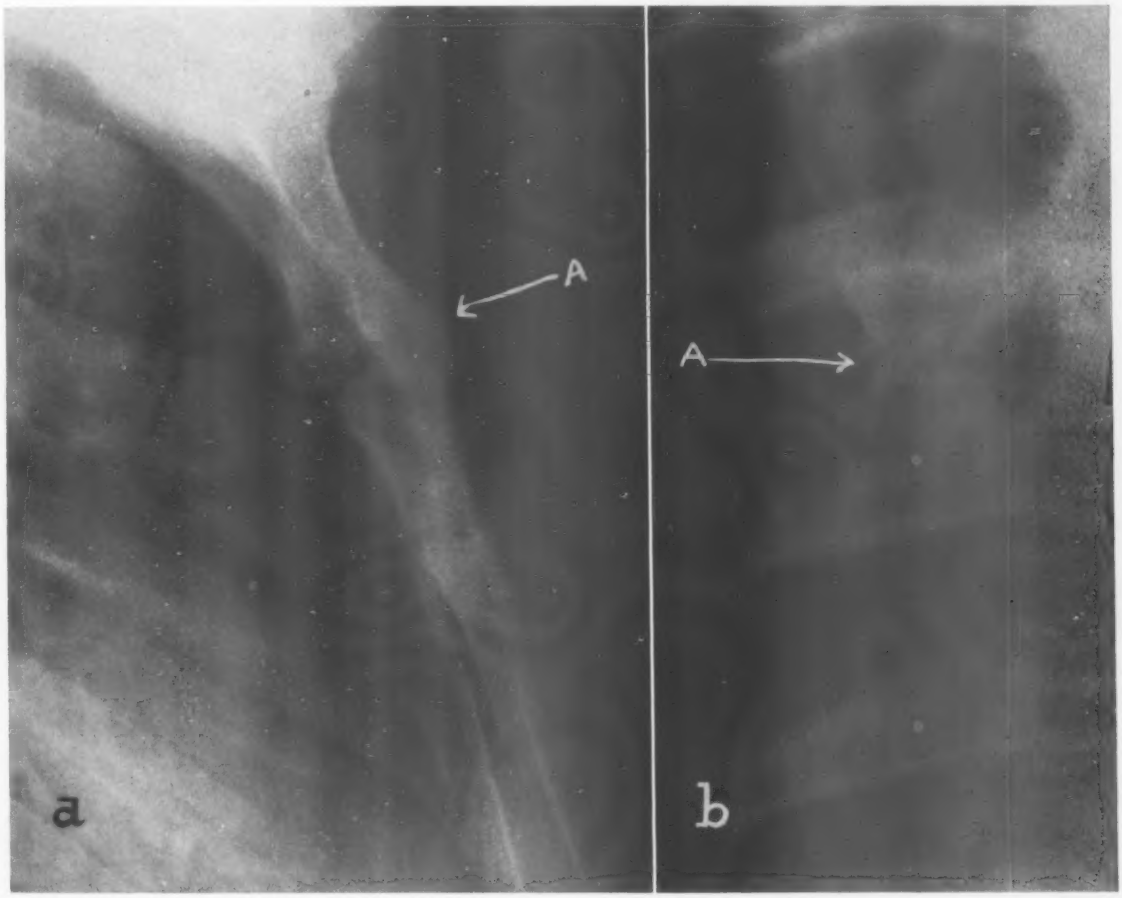

Fig. 6. (*a*) and (*b*). October 20, 1949. W. T. P., twenty-eight year old white male with onset of rheumatoid spondylitis in 1945. Now lower dorsal and lumbosacral spine and both knees are affected. (A) Irregularity, increased density and partial obliteration of manubriosternal joint.

In 6 of the more recently examined patients, oblique views of the sternum, in addition to the lateral views, were obtained, and these showed the erosive and productive changes of this joint to much better advantage. One of these sternums had shaggy margins similar to the periosteal excrescences sometimes noted in the pelvis.

CONCLUSIONS

1. Fusion of the manubriosternal joint

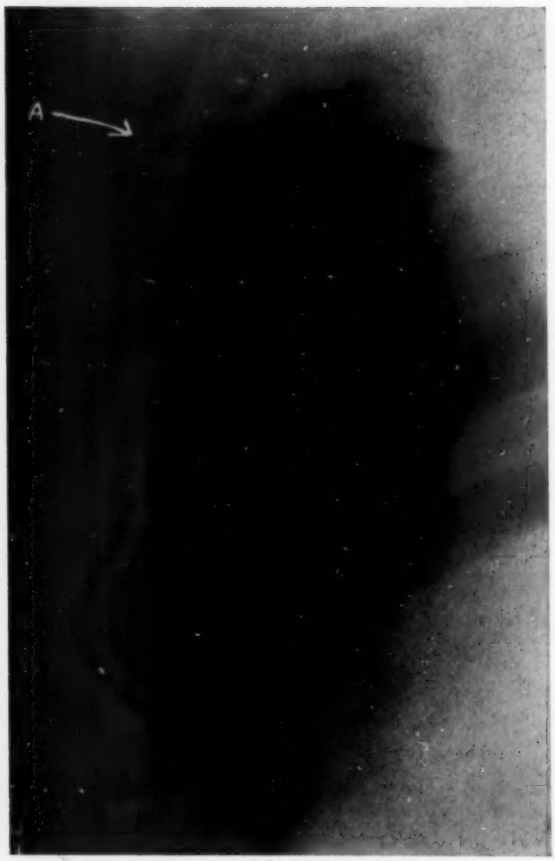

FIG. 7. July 11, 1946. O. T., fifty-three year old white male. Onset of spondylitis in 1941. Now has "poker" back. (A) Erosion of articular surfaces. Apparent calcification of ligaments at margins of sternum.

is noted in younger as well as in older individuals without rheumatoid spondylitis. It occurs in 5.5 per cent of our patients, and in 6 per cent of Zimmer's cases.[19] We agree with Zimmer that it is a developmental variation, except where secondary to local disease, rather than a manifestation of senescence.[2]

2. Fusion of the manubriosternal joint is four times more frequent in Marie-Strümpell disease (23 per cent) than in non-rheumatoid disease of the spine (5.5 per cent) in our series of cases. It is suggested that there is an increased susceptibility to ankylosis of this joint in this disease possibly as an end result of active rheumatoid arthritis of this joint. This hypothesis is given support by the finding of:

3. Erosive changes, subarticular increase in density and evidences of beginning obliteration of this articulation in 9 other patients with spondylitis rhizomelique. Since rheumatoid arthritis is known to affect synovial joints primarily, the anatomical fact that a third of the manubriosternal articulations develop synovial cavities[8a] may have a bearing on the involvement of this joint in some cases of Marie-Strümpell disease. In this connection, it is of interest that the symphysis pubis, which sometimes contains a synovial cavity, is occasionally involved in this disease and the intervertebral discs, which never contain a synovial cavity, are never involved.

4. Many patients with spondylitis rhizomelique complain of pain and soreness in the anterior chest. These complaints are frequently attributed to psychoneurosis or cardiac disease. Pathological involvement of the sternum or manubriosternal joint should be considered in evaluating these symptoms.

DIFFERENTIAL DIAGNOSIS

1. Considerable irregularity of the articular margins of the manubriosternal joint may be present due to unequal growth of the ossification centers during the developmental period.[11,19] There may be small defects in the articular surfaces which have been considered to be analogous to Schmorl's nodes,[19] but which may be developmental also. These defects and irregularities have clear-cut margins and do not resemble the ragged erosions with underlying increase in density noted in rheumatoid arthritis.

2. Narrowing of the joint space, osteophyte formation and bridging of the osteophytes may occur in old age, as in hypertrophic arthritis of the vertebrae. The joint space, though thin and sometimes obliterated at its periphery, has smooth margins.

3. A poorly defined condition which has a roentgenological picture similar to that observed by us, but not associated with rheumatoid disease of the spine, and desig-

nated as chondritis and perichondritis has been described in 2 cases.[19]

4. Other forms of infectious or metabolic arthritis may conceivably involve this joint, with similar roentgenological findings.

5. Tuberculosis may occur as a sequestrating osteomyelitis or an osteoperiostitis.

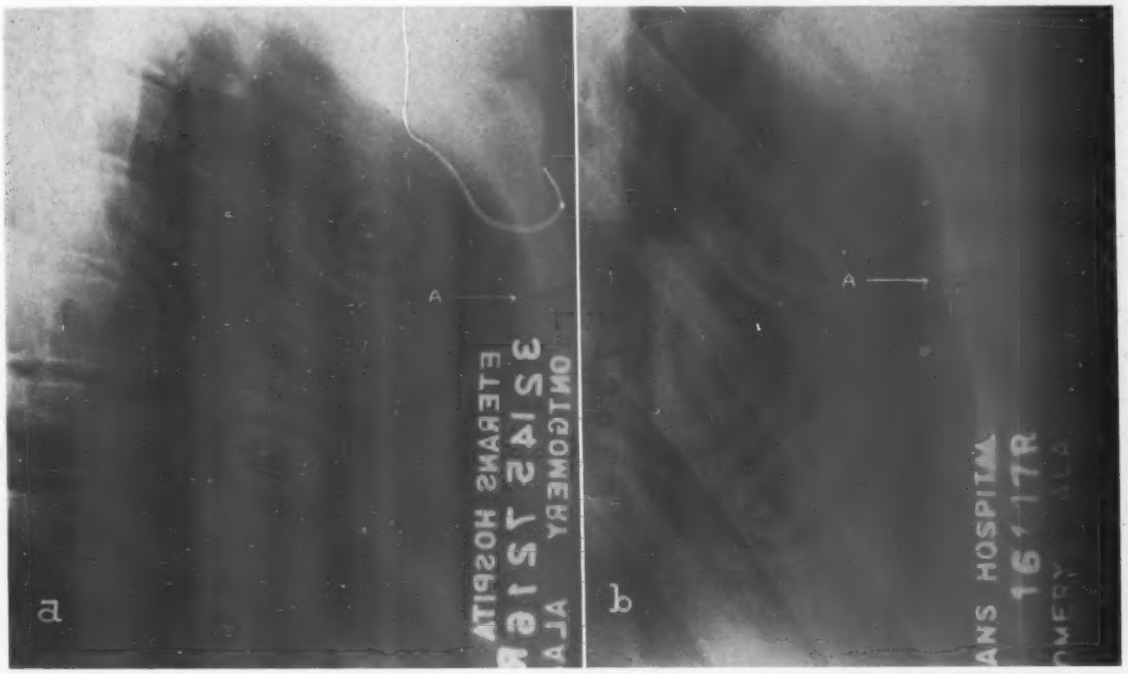

Fig. 8. H. R. P., thirty-one year old white male with onset of rheumatoid spondylitis in 1942. Entire spine now involved. (*a*) March 21, 1945. (A) Normal manubriosternal joint. (*b*) December 2, 1947. (A) Characteristic changes of rheumatoid arthritis now present.

It is localized near joints and leads to ring-shaped foci mostly in the body of the sternum, less often in the manubrium.[14] The disease process may go right up to the manubriosternal joint and rapidly lead to destruction and eventually also to luxation of this joint.[19]

6. Destructive changes in the manubrium or body of the sternum, possibly adjacent to the manubriosternal joint, may be due to various neoplastic diseases such as metastatic carcinoma, multiple myeloma, and lymphoma. These should be difficult to confuse with the pathological process described in this paper.

TECHNIQUE

Pathological processes in the sternum as a whole or in the manubriosternal joint, in particular, have not received much attention because of the difficulty in roentgen visualization of these structures. To obtain an oblique view of the sternum, the following technique was devised by James L. Crowder, R. T. of our department. It was found to give a satisfactory image of the sternum in most cases. The patient is placed in a prone oblique position with the left arm by the side and the right arm elevated over the head, the face resting on the right forearm. The body is rotated slightly to separate the sternum from the shadow of the spine. In order to blur the images of the ribs and lungs, the patient is allowed to breathe quietly and the cone is brought down in contact with the patient. Due to the short target to film distance, shock-proof equipment is required. In case the patient cannot hold still, immobilization may be obtained by use of a compression band drawn across the thorax.

A size 8 by 10 inch screen film in a cardboard film holder is used in the Potter-

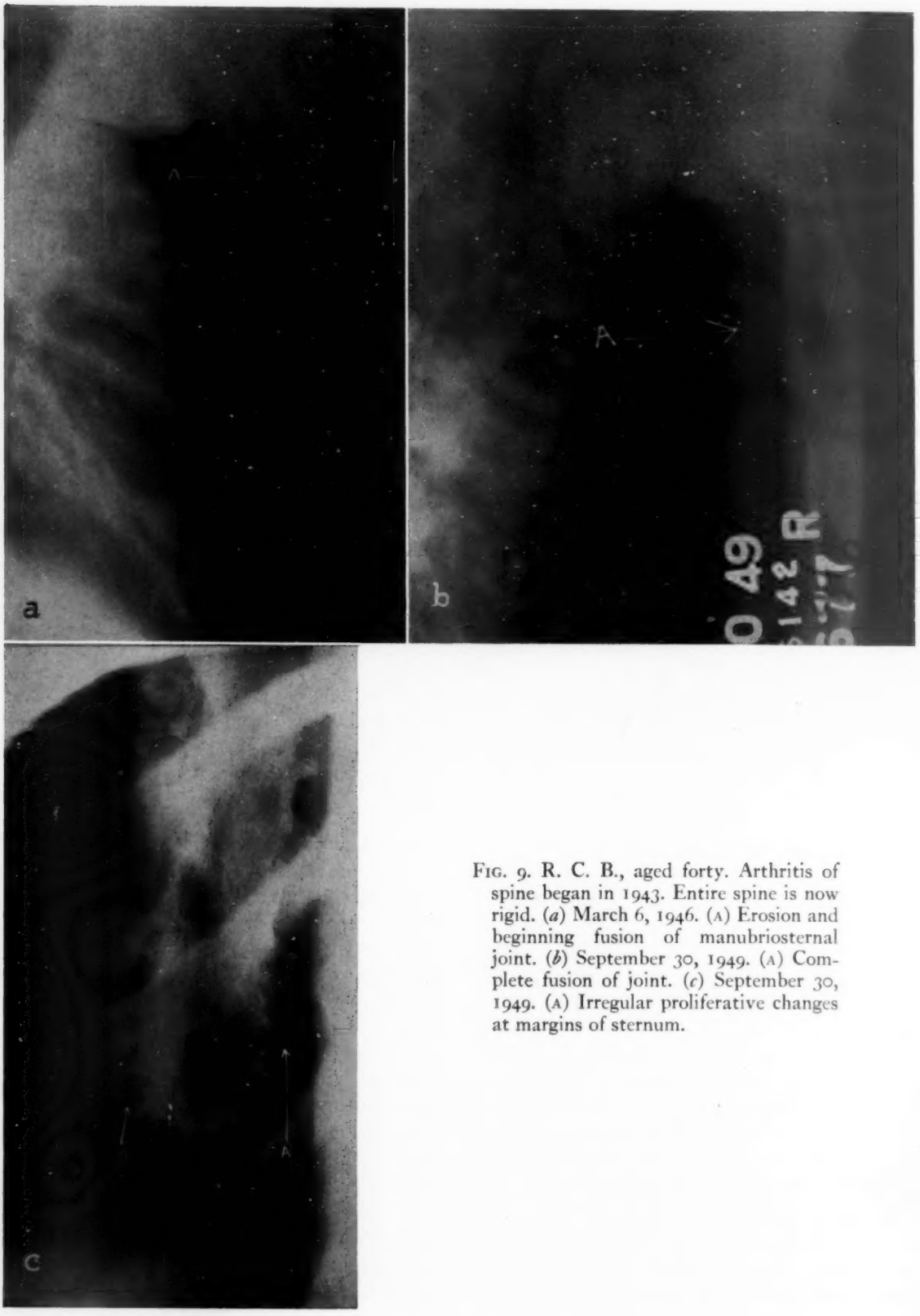

FIG. 9. R. C. B., aged forty. Arthritis of spine began in 1943. Entire spine is now rigid. (*a*) March 6, 1946. (A) Erosion and beginning fusion of manubriosternal joint. (*b*) September 30, 1949. (A) Complete fusion of joint. (*c*) September 30, 1949. (A) Irregular proliferative changes at margins of sternum.

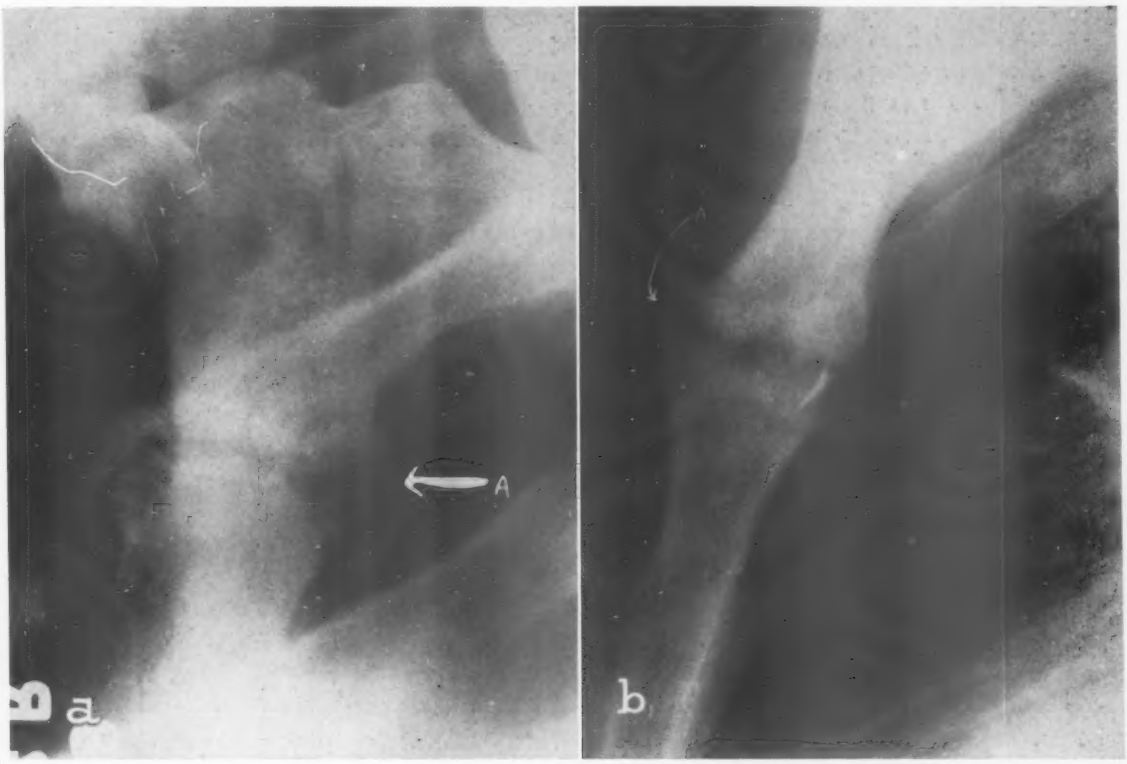

Fig. 10. August 21, 1949. O. C., thirty-four year old white male. Onset of spondylitis rhizomelique in 1947. Now has moderately advanced arthritis of dorsal and lumbosacral spine. Has noticed enlargement and some tenderness at angle of Ludwig. (*a*) (A) Erosion and proliferative changes at margins of manubriosternal joint. (*b*) (A) Osteophyte formation indicating hypertrophic in addition to atrophic arthritis.

Bucky diaphragm. The upper end of the film holder is placed 1 inch above the suprasternal notch. The sternum is exactly in the center of the roentgen table, and the central ray is projected through the thorax to the left of the spine and perpendicular to the center of the film. If the manubriosternal articulation is found to be overshadowed by a posterior rib, the patient's head and shoulders are bent forward into a stooping position.

Factors employed were:

Cm.	Ma.	Time	Kv. (peak)	Distance	Degree of Rotation
23	30	12 sec.	66	Cone	12°
27	30	12 sec.	74	Cone	8°

SUMMARY

1. Pathological involvement of the manubriosternal joint has not been described in Marie-Strümpell disease or in the peripheral type of rheumatoid arthritis, probably because of the difficulty in the roentgen visualization of the sternum.

2. Anatomically, the manubriosternal joint is an amphiarthroidal joint with fibrocartilage between the bone ends, but about one-third of the cases develop a synovial cavity.

3. Fusion of the manubriosternal joint in cases without rheumatoid spondylitis is probably a developmental variation, in the absence of local disease, rather than due to senescence as commonly believed. It occurs in about 6 per cent of the sternums.

4. Fusion of the manubriosternal joint in Marie-Strümpell disease in our series (57 cases) is four times as frequent as in non-rheumatoid spines (580 cases).

5. Erosive changes, increased density of the subarticular bone and evidences of beginning fusion were noted in 15.8 per cent

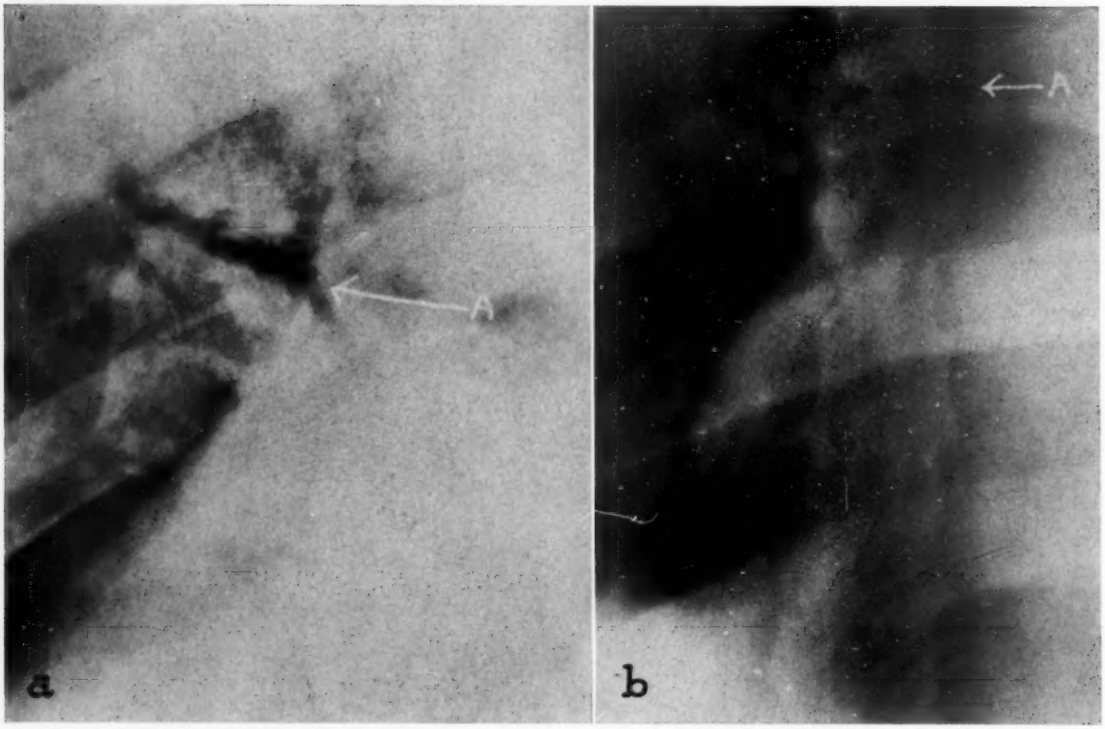

FIG. 11. R. F. A., twenty-nine year old white male. Onset of rheumatoid spondylitis in 1943. Has had periodic pain and swelling at the angle of Ludwig since onset, and residual tenderness between episodes. At present, he has moderate involvement of the lumbosacral spine. (*a*) March 18, 1947. (A) Slight erosion and increased density at manubriosternal joint. (*b*) September 26, 1949. (A) Failure of fusion of joint after six years of pathological involvement.

of our 57 cases of spondylitis rhizomelique. These changes in the manubriosternal articulation are believed to be manifestations of rheumatoid arthritis. In this connection, it is of interest that a third of these joints have synovial cavities, that the symphysis pubis which sometimes contains a synovial cavity is rarely involved in this disease, and that the intervertebral disc which never contains a synovial cavity is never involved.

6. Differential diagnosis includes developmental irregularity of the articular margins of this joint, narrowing of the joint space, and osteophyte formation due to degenerative arthritis, chondritis and perichondritis, infectious or metabolic arthritis, tuberculosis and neoplastic disease.

We wish to acknowledge the efforts of James L. Crowder, R.T., for his interest in devising a technique for roentgenography of the sternum.

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PELVIC AND EXTRAPELVIC OSTEOPATHY IN RHEUMATOID SPONDYLITIS*†

A CLINICAL AND ROENTGENOGRAPHIC STUDY OF NINETY CASES

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INTRODUCTION

COMPARATIVELY little attention has been given to the abnormal roentgenographic changes so often seen in the bones of the pelvic girdle in patients with rheumatoid spondylitis. No symptoms have been attributed to them. They have been given passing mention by a few authors who have maintained that such changes occur but rarely and only late in the disease.

Krebs and Vontz[10] were the first to describe patchy areas of increased density in the ischia and pubes with roughening of the periosteum. They also observed exostosis formation and "ulcerous defects" in the symphysis pubis. Golding[9] noted "a peculiar manifestation of the disease (spondylitis ankylopoietica) . . . in the soft bones . . . found as a rare event in advanced cases in the ischial tuberosity, the patella and os calcis." He was undecided as to the nature of these changes and admitted that they would be difficult to interpret if they were seen apart from the spinal condition. Dunham and Kautz[6] reported such changes in the ischia, pubes and iliac crests in 15 of their 20 cases. Three of the 15 had no demonstrable calcification in the paraspinal ligaments. One patient had low back pain for only three and one-half years, had no paraspinal ligamentous calcification, but did have roentgenographic findings in the ischia, pubes and iliac crests similar to those described above. These authors were of the opinion that the changes in the pelvic girdle were of the same nature as those seen in the bone about the apophyseal and sacroiliac joints. Oppenheimer[12] found "irregular bony spikes" projecting from the inferior margins of the pubic and ischial bones in 3 of 53 patients, and "complete ossification" of the symphysis pubis in 2 patients. Borak[4] was of the opinion that the "osteosclerosis" adjacent to the sacroiliac joints represents an adaptation to stress imposed by inflammatory disease of the lumbar apophyseal joints. He also believed that the increased calcification about the pelvic girdle is a late manifestation of the same adaptive process and is not inflammatory in origin. In support of this contention was his observation that the changes about the sacroiliac joints and pelvic girdle were symmetrical. Boland and Shebesta[2] noted the "ragged margins" of the symphysis pubis which "occasionally" may be involved, and stated that "involvement of the ischial tuberosities is but rarely seen." Polley[13] and Boland,[3] among others, have never observed any essential change in the structure of the vertebral bodies other than diffuse osteoporosis.

In a study of 90 patients with rheumatoid spondylitis, abnormal findings were commonly seen in the roentgenograms of the pelvic bones and were often accompanied by symptoms. Usually they oc-

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curred in patients with advanced disease but they were occasionally present in those with early disease. Sometimes they were associated with similar changes in extrapelvic osseous structures, including the vertebral bodies. Rarely were similar changes noted in extrapelvic osseous structures in patients without demonstrable abnormality about the periphery of the pelvic girdle.

NATURE OF THE MATERIAL

A total of 90 patients with rheumatoid spondylitis were studied at the Bronx Veterans Administration Hospital. Only those cases were included who had an unequivocal diagnosis of rheumatoid spondylitis and whose roentgenograms were considered satisfactory and complete enough for the purposes of this study. These cases were unselected. The changes ascribed to osteopathy in the pelvic girdle and elsewhere are definitive, gross, and obvious ones. Those cases with equivocal changes were considered not to have osteopathy.

CLINICAL FEATURES

Adequate histories and physical examinations with reference to the bones of the pelvis were obtained in 49 patients. Eighty-six per cent experienced tenderness in these bones at one time or another (Table 1). Most patients referred to the tenderness as "hip pain," but some volunteered the information that they had discomfort while sitting in a chair. Only 8 of the 49 patients had abnormal roentgenographic changes in or about the hip joints, and 2 of these never experienced pelvic bone tenderness. By careful questioning, it was possible to differentiate the pain, tenderness and limitation of motion due to disease in the hips from the discomfort caused by disease in the bones of the pelvis. Polley[13] commented on the "hip pain" reported by patients who misname the anatomical site of their discomfort. The tenderness appeared to be in the pelvic bones themselves and was elicited by firm but gentle pressure. It was

FIG. 1. Twenty-six year old white male, with pain and tenderness in the left buttock for five years and low back pain for two years. The roentgenogram shows osseous eburnation and lytic defects, with irregularity of contour of the left ischial tuberosity simulating osteomyelitis. Also note the increase in density of the pubic bones near the symphysis and the changes about the sacroiliac joints indicative of rheumatoid spondylitis. The lumbar apophyseal joints were involved roentgenographically. A biopsy of the left ischial lesion, performed at another hospital, showed "chronic sclerosing osteitis."

TABLE I

CLINICAL FEATURES: BONE TENDERNESS

	Number of Patients		
	Pelvic Girdle	Sternum	Ribs
Positive history—negative physical	8	6	5
Positive physical—negative history	2	3	3
Positive history and physical	32	14	14
Total with tenderness	(42)	(23)	(22)
Negative history and physical	7	14	14
Total number of patients	49	37	36

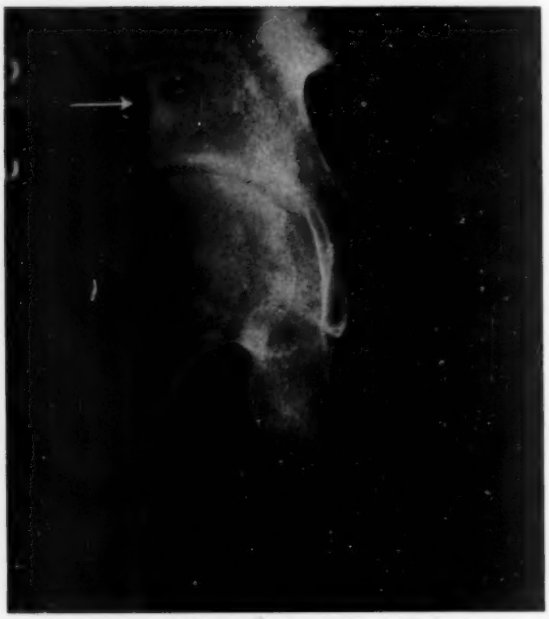

FIG. 2. Twenty-four year old white male, with a three year history of low back pain. The roentgenogram shows the presence of two lytic defects in the lower third and the outer margin of the right iliac bone, probably due to "rheumatoid nodules." Note the changes in the right sacroiliac joints and right ischial tuberosity characteristic of rheumatoid spondylitis.

found in one or more of the following: the symphysis pubis, pubic rami, ischial tuberosities, and the iliac crests. It was usually well localized and was intermittent, waxing and waning with the other symptoms of the disease. It preceded the onset of low back pain in 2 patients, in 1 by three and one-half years, and in the other, by two years. It was experienced simultaneously with the onset of low back pain by 13 patients. However in most patients it followed the development of low back pain. The average interval between the onset of low back pain and pelvic tenderness (excluding the 15 patients mentioned above) was five and one-half years. Four of 7 patients, who had never experienced tenderness in the pelvic girdle, had abnormal roentgenographic changes in their pelves. Eight patients, who had pelvic tenderness, showed no abnormal roentgenographic changes in their pelves other than those about the sacroiliac joints. Two of the latter group had experienced symptoms for only a few months, but the remaining 6 had tenderness for from two to thirteen years. The ischial tuberosities were most frequently tender. Tenderness often occurred in more than one of the pelvic bones (Table II).

TABLE II

CLINICAL FEATURES

Site of Pelvic Tenderness	Number of Times Involved
Ischial tuberosities	33
Iliac crests	23
Symphysis pubis	15
Pubic bones below symphysis	12

Adequate histories and physical examinations with reference to the sternum and ribs were obtained in 37 and 36 patients respectively. Tenderness occurred at these sites in approximately 60 per cent of these patients (Table I). Rib and sternal tenderness were not associated with each other in all patients. Tenderness was of the same quality as that which was elicited in the pelvic bones. It was often present in the lower ribs, but was also found elsewhere in the anterior chest and axillae. Frequently it was limited to a small area in one rib. The discomfort did not resemble that which is usually attributed to radicular pain. Pain was often absent when tenderness was present.

NATURE OF THE ROENTGENOGRAPHIC CHANGES

The roentgenographic changes suggesting osteopathy consisted of the following: (1) irregular lytic defects which had a punched out appearance in the pelvic and extrapelvic osseous structures; (2) irregular zones of increased bone density; (3) "whiskering" or "fringing" of the periphery of bone. The first two changes resemble those seen in the vicinity of the sacroiliac and apophyseal joints in rheumatoid spondylitis as well as those seen in bone adjacent to involved joints in peripheral rheumatoid disease. The "whiskering" suggested peri-

tendinitis (bursal, ligamentous, or tendon involvement), or periostitis and osteitis. It is possible that a combination of these factors is responsible for this change.

PELVIC OSTEOPATHY
(Fig. 1, 2, 3, 4, 5, 6)

Of 90 patients studied, 74.4 per cent were found to have abnormal roentgenographic changes in their pelvic bones which are described in the previous paragraph. The majority of this group had moderately to severely advanced disease, as manifested by paraspinal ligamentous calcification, but a significant minority had early disease as judged by this criterion (Table III). The extent of the changes in the pelvic bones paralleled the severity and extent of the spondylitis. The average duration of back symptoms in 52 patients who had roentgenographic evidence of osteopathy limited to the pelvic girdle was approximately eight years (Table IV). The majority had had back symptoms for four years or longer. None of the patients had back symptoms for less than one year, 6 had them for two years or less, and 10, for three years or less.

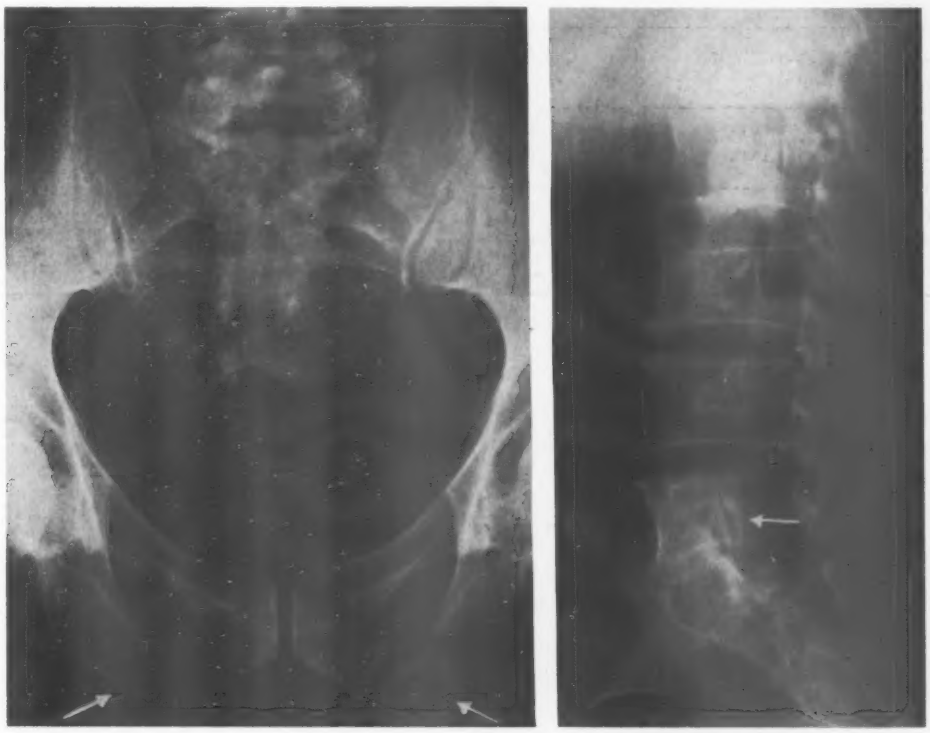

FIG. 3. Thirty-five year old white male, with a five year history of low back pain and ischial tuberosity tenderness. The roentgenograms show whiskering, irregularity and lytic defects in the outer margins of each ischial tuberosity. The sacroiliac joints appear normal. The oblique view of the lumbar apophyseal joints show rheumatoid involvement between the articulating surfaces of the fifth lumbar and first sacral vertebrae. Involvement of the lower dorsal and upper lumbar apophyseal joints is also present but not well demonstrated in this reproduction. Paraspinal ligamentous calcification was observed in other roentgenograms.

Twenty-five of 26 patients in this group who were adequately questioned and examined had pelvic tenderness (history or physical examination), usually in the area seen to be involved in the roentgenograms. The ischial tuberosities were most frequently involved. Abnormal findings were usually multiple, and were bilateral and symmetrical in most. However, there was a significant number in which this did not obtain (Table V).

TABLE III

ROENTGENOGRAHPIC FEATURES

The correlation of the frequency of pelvic girdle osteopathy to the severity of the disease as judged by paraspinal ligamentous calcification

	Number of Patients				
	Osteopathy Pelvic Girdle	Extrapelvic and Pelvic Osteopathy	Extrapelvic Osteopathy	No Osteopathy	Total Number of Patients
No paraspinal ligamentous calcification	9	1	0	13	23
Slight to moderately advanced ligamentous calcification	24	6	2	6	38
"Bamboo spine"	19	8	1	1	29
Total number of patients	52	15	3	20	90

TABLE IV

ROENTGENOGRAPHIC FEATURES

Duration of the disease (measured by onset of low back pain) and its relation to osteopathy and paraspinal ligamentous calcification

Duration Back Symptoms —Years	No Osteopathy	Osteopathy Pelvic Girdle Only	Osteopathy Extra-pelvic and Pelvic	Osteopathy Extra-pelvic Only	No Ligamentous Calcification	Slight to Moderate Ligamentous Calcification	"Bamboo Spine"	Total Number of Patients
Average —Years	5.2	8.1	13.2	6				
Less than 1	2	0	2	0	3	1	0	4
1– 2	2	3	0	0	4	1	0	5
2	0	3	0	0	2	0	1	3
3	1	4	0	0	0	4	1	5
4	0	10	0	0	3	5	2	10
5	7	7	2	0	6	5	5	16
6	2	6	2	2	2	6	4	12
7	0	2	1	1	0	3	1	4
8	0	2	0	0	0	0	2	2
9	2	2	0	0	0	3	1	4
10	0	2	1	0	0	2	1	3
11–15	2	1	0	0	1	2	0	3
16–19	0	1	1	0	1	1	0	2
20 plus	0	7	5	0	0	2	10	12
Unknown	2	2	1	0	1	3	1	5
Total number of patients	20	52	15	3	23	38	29	90

EXTRAPELVIC OSTEOPATHY
(Fig. 7 and 8)

Osteopathy in areas other than the pelvic bones was observed in 18 of 90 patients. Fifteen of this group had roentgenographic evidence of disease in the pelvic girdle as well. Osteopathy was observed in the vertebral bodies in 7 different patients (Fig. 7). Similar changes were found in the femurs, head of the humerus, acromion, carpal bones, sternal notch, angles of the scapulae, elbow, lower ends of the tibia and fibula, toes, and a patella. The average duration of back symptoms in this group was more than thirteen years, and all but one had

TABLE V

ROENTGENOGRAPHIC FEATURES: SITES OF INVOLVEMENT IN THE PELVIC GIRDLE

	Number of Cases	
Ischial tuberosities alone	11	
Unilateral 3		
Bilateral 8		
Pubic bones alone	6	
Symphysis 5		
Below symphysis (bilateral) 1		
Iliac crests alone	0	
		17 = Total with one group of bones involved
Two groups of bones involved	23	
Bilateral and symmetrical 15		
Not bilateral and symmetrical 8		
All pelvic bones involved	27	
Bilateral and symmetrical 17		
Not bilateral and symmetrical 10		
		50 = Total with multiple joint involvement
		67 = Total patients with pelvic osteopathy

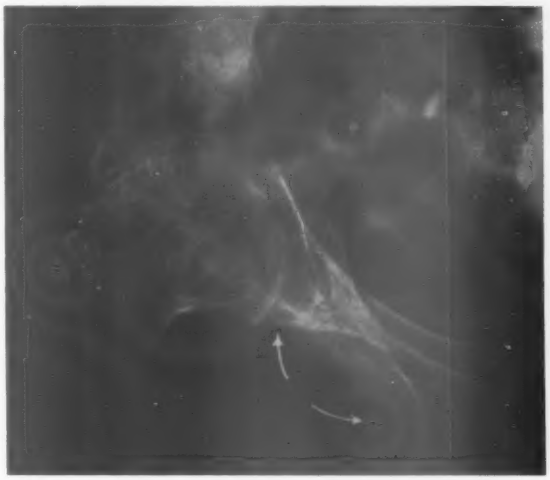

FIG. 4. The roentgenogram demonstrates marked irregularity, bony proliferation and lytic defects with eburnation of the right ischial tuberosity. Note the narrowing of the right hip joint with bony decalcification. The changes of rheumatoid spondylitis were demonstrated in this patient in the sacroiliac and lumbar apophyseal joints.

FIG. 5. The roentgenogram shows proliferative changes and irregular lytic defects of the ischial tuberosities and the outer aspects of the iliac bones just above the middle third. Note also the changes in the sacroiliac region characteristic of rheumatoid spondylitis.

FIG. 6. The roentgenogram shows lytic defects and bony proliferation with eburnation of the ischial tuberosities, as well as eburnation of both pubic bones below the symphysis. Note also the changes characteristic of rheumatoid spondylitis in the sacroiliac region, as well as paraspinal ligamentous calcification.

paraspinal ligamentous calcification (Tables III and IV). No cause for these findings, other than rheumatoid disease, was demonstrated in any of these patients.

Only 3 patients had osteopathy in extrapelvic osseous structures who did not have demonstrable pelvic lesions. All had paraspinal ligamentous calcification and all had back symptoms for six years or longer. In these 3 patients, individual lower dorsal vertebral bodies were involved.

NO PELVIC OR EXTRAPELVIC OSTEOPATHY DEMONSTRABLE ON ROENTGENOGRAPHIC EXAMINATION

Of the 90 patients, 22.2 per cent had no abnormal changes in pelvic and extrapelvic osseous structures although they showed the characteristic changes of rheumatoid spondylitis in their sacroiliac and apophyseal joints (Tables III and IV). The majority of this group demonstrated no paraspinal ligamentous calcification, and the average duration of back symptoms was only five years. Two patients reported pelvic tenderness for less than one year, 1 for two years, and 3 for variable periods (four to thirteen years). In 10 instances no mention was made of this symptom in the hospital records; however, it may not have been particularly looked for by the examining physicians. One patient never complained of back or pelvic symptoms, but he did have the characteristic changes of rheumatoid spondylitis in his sacroiliac and apophyseal joints which were discovered quite by accident.

PERIPHERAL ARTHRITIS

Arthritis of peripheral joints (excluding

FIG. 7. Fifty-two year old white male, with peripheral rheumatoid arthritis and spondylitis for twenty-four years. The roentgenogram shows a ragged, destructive lesion involving the adjacent surfaces of the anterior surface of the bodies of the eleventh and twelfth thoracic vertebrae with peripheral eburnation and disc space narrowing (not unlike tuberculous spondylitis). Diagnostic studies revealed no other cause for this lesion. Note artefact over inferior one-half of the body of the twelfth thoracic vertebra.

hips, temporomandibular joints, and shoulders) occurred in 47 (56.6 per cent) of 83 patients who were adequately questioned and examined. Twenty of these had bilateral and symmetrical joint disease which was indistinguishable from "classical" rheumatoid arthritis. Those listed as "atypical arthritis" had a history of acute peripheral joint inflammation or had objective evidence of arthritis which was not bilateral and symmetrical. There appeared to be no relationship of pelvic and spinal osteopathy to peripheral arthritis (Table VI).

Only 19 of 90 patients (21 per cent), who had roentgenograms of the hips, showed arthritis in these joints. Thirteen of 58 patients had roentgenographic evidence of arthritis in the shoulder girdle; in most of these, the changes were limited to the acromioclavicular joints. It is of interest that pelvic bone disease was demonstrated more frequently than was hip or shoulder disease in patients with rheumatoid spondylitis.

FIG. 8. The roentgenogram demonstrates irregularity of contour, lytic defects of the right transverse process of the fifth lumbar vertebra. Note the changes about the right sacroiliac joint. Diagnostic studies revealed no other cause for this lesion. Complete roentgenographic study revealed the changes typical of rheumatoid spondylitis.

DISCUSSION

Marie and Léri[11] and Buckley[5] considered spondylitis to be primarily an infectious or toxic osteopathy. The report of a necropsy by Fagge[7] has been cited[5] as support for this hypothesis. It is not contended here that the disease is primarily an osteopathy. The pathological material, which has been examined and reported,[1,8,13] has revealed changes within the apophyseal and peripheral joints which are indistinguishable from those found in rheumatoid arthritis. The material herein reported merely indicates that bone lesions are frequently demonstrable in patients with rheumatoid spondylitis.

This study suggests that the osteopathy represents an inflammatory rather than an adaptive process as was maintained by Borak.[4] This contention is supported by: (1) the tenderness which was found in the bones of the pelvis; (2) the report of "chronic sclerosing osteitis" on material obtained from a biopsy of an involved ischial tuberosity (Fig. 1); (3) the occurrence of lytic defects and proliferative changes in the ischial tuberosity of a patient who had apophyseal joint changes

TABLE VI

CLINICAL FEATURES

Relation of peripheral arthritis to pelvic and extrapelvic osteopathy

	No Peripheral Arthritis	Atypical Arthritis	Typical Arthritis
Patients with rheumatoid spondylitis without osteopathy	10	8	2
With osteopathy pelvic girdle	28	13	11
With osteopathy pelvic and extrapelvic structures	2	6	7
Total number of patients	40	27	20

and paraspinal ligamentous calcification, characteristic of rheumatoid spondylitis, but who did not have roentgenographic evidence of bone condensation in the neighborhood of the sacroiliac joints (Fig. 3).

The roentgenographic findings herein described are not unlike those which are frequently seen in bone adjacent to diseased joints in patients with peripheral rheumatoid arthritis. It is probable that these changes are of the same nature. The changes found in the pelves, vertebral bodies, and transverse processes of the vertebrae also resembled those which were found peripherally in those patients who showed combined peripheral and spinal arthritis. These findings further suggest that rheumatoid spondylitis is but the spinal variant of rheumatoid arthritis.

The oft-repeated statement that the vertebral bodies are not involved by this disease, except for diffuse osteoporosis, is negated by the demonstration of osteopathy of the vertebral bodies in 7 patients. Three patients had destructive lesions in the transverse processes of their vertebrae. Nineteen of the 90 patients had narrowing of their intervertebral disc spaces, a finding also noted by Dunham and Kautz.[6]

Tenderness of the sternum, ribs, and clavicles suggests that these may be the sites of osteopathy. In one patient there were roentgenographic changes in the sternal notch suggestive of osteopathy. Occasionally changes were noted in the acromion, but not in the clavicles or ribs.

Roentgenographic evidence of hip and shoulder disease was much less frequently seen than was disease of the pelvic girdle. A number of patients with peripheral rheumatoid arthritis and rheumatoid spondylitis had roentgenographic findings of osteopathy in the bones of the extremities, as well as in the pelvis.

SUMMARY

1. Pelvic osteopathy, manifested by clinical and roentgenographic findings, is a common feature of rheumatoid spondylitis.

2. Extrapelvic osteopathy also occurs.

3. The vertebral bodies and transverse processes of the vertebrae are occasionally involved.

4. The roentgenographic changes in rheumatoid spondylitis, which are described, are similar to those seen in rheumatoid arthritis, with or without spondylitis.

5. The evidence suggests that these changes are inflammatory rather than adaptive.

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Vol. 65, No. 5

SYNOVIOMA

WITH SPECIAL REFERENCE TO THE CLINICAL AND ROENTGENOLOGIC ASPECTS*

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TO DATE approximately 100 cases of synovioma have been reported in the literature. For the most part the pathology of the tumor has been stressed,[1,3,7] and little has been written on the clinical and roentgenologic aspects of this rare disease. It is the purpose of this paper to present 17 cases of synovioma which have been observed at the Massachusetts General Hospital during the past sixteen years, and to point out the salient features of the clinical and roentgenologic aspects of this type of neoplasm.

PRESENTATION OF MATERIAL

Out of 650,000 hospital admissions from 1933 through 1948, there were 17 cases of histopathologically proved synovioma. All the patients were white; 10 were females and 7 males. Their ages ranged from four to sixty-five years with an average age of thirty-one and a median age of twenty-nine.

A history of trauma as a predisposing factor in approximately 25 per cent of cases of synovioma has been suggested by other investigators.[1,5,6] In this group, however, in only 4 instances was there even a vague history of trauma, and in but 1 was it considered a reliable observation. In this case the injury had been received three months before the tumor was detected; in the other 3, an interval of from three to seven years had elapsed between the time of the trauma and the appearance of the tumor. The usual history was that of a mild ache or pain, sometimes associated with stiffness of the affected part. The duration of symptoms varied from two months to six years, with an average duration of two years.

The chief physical sign was a non-tender firm mass in or near a joint. In all but 2 of the 12 patients who exhibited such a swelling, it was described as freely movable; in these 2, the duration prior to the establishment of the diagnosis had been three and five years respectively. In the latter (Case III), the tumor had remained stationary for four years, at which time it began to grow rapidly in size. This case was unusual in another respect as it was the only one in the group which showed signs of inflammation on physical examination.

Nine of the 17 patients had received their primary treatment before admission to this hospital; it had consisted of simple excision in 8 and of roentgen irradiation in one. A preoperative diagnosis of malignant tumor was considered in only 9 of the 17 cases. The diagnoses in the remaining 8 included tuberculous adenitis, subdeltoid bursitis, inguinal hernia, myositis ossificans, lipoma, and ruptured medial meniscus. In approximately one-half of the group, therefore, the seriousness of the condition was not recognized until the biopsy specimen had been examined microscopically. Even after the diagnosis had been established, because the tumor was encapsulated and was easily removed by blunt dissection, the serious prognosis was not always recognized. Case I illustrates this point:

A woman, aged sixty-five, was admitted with a small mass on the medial aspect of the knee; the mass was non-tender and freely movable and had been present for one year. The roentgenograms revealed a soft tissue mass, and the diagnosis suggested was synovioma, or possibly sarcoma. At an exploratory operation, the tumor was found to be encapsulated, seemingly limited to the capsule. Blunt dis-

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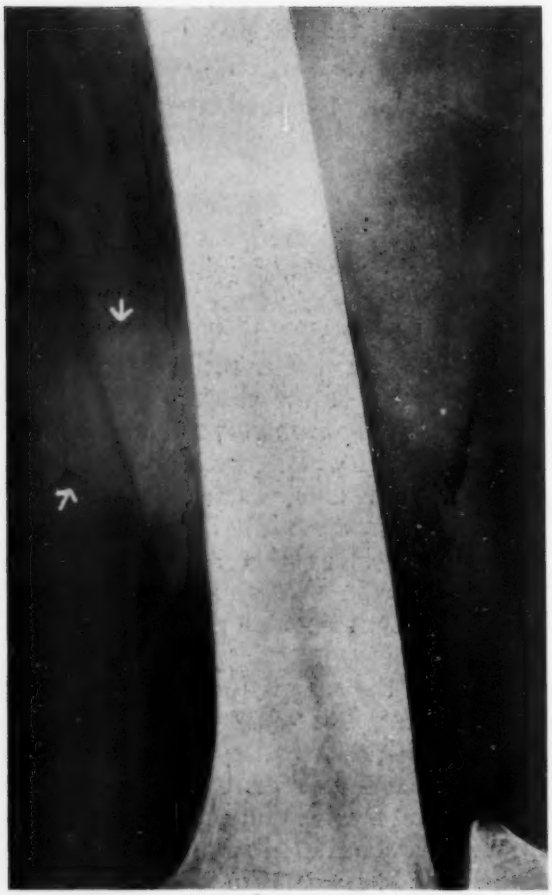

Fig. 1. Case VIII. Synovioma of thigh. Note the smooth soft tissue mass on the posterior lateral aspect of the thigh.

section was easily accomplished and the tumor was enucleated locally. During the course of the dissection the question was raised as to whether the capsule of the tumor had been broken into at one point. Eight months after operation, the patient developed signs of neurologic involvement; two months later, roentgen examination showed pulmonary metastases; and one year postoperative, the patient died.

ROENTGENOLOGIC ASPECTS

An accurate diagnosis of synovioma cannot be made on the roentgenologic findings alone. It is highly suggestive, however, when a soft tissue mass in a joint (Fig. 4), or near a joint, is lobulated and contains a fine, speckled type of calcium which is laid down in small rounded masses, irregularly arranged. In 9 of the 10 cases in which roentgenograms were available, a soft tissue mass is described (Fig. 1). In 4 of these, the mass was discrete and lobulated; in 5, calcification as previously described was observed (Fig. 2). In 1 case showing calcium, periosteal proliferation was also evident; in another case in which no calcium was noted, there was a break in the cortex with periosteal proliferation and deformity of the bone from extrinsic pressure (Fig. 3).

At a later stage in the disease, pulmonary metastases, when present, were readily demonstrable (Fig. 8). They were present in all of the 11 fatal cases. A much more unusual finding from the roentgenologic standpoint was the development of bone metastases remote from the original site of the tumor in 3 of the group. Two of the 3 came to autopsy. An incidence of 18 per cent of bone metastases is of interest when

Fig. 2. Case VII. Synovioma of thigh. The soft tissue mass contains a speckled type of calcification, irregularly arranged. This is a rather frequent roentgenologic finding in this type of tumor.

compared to that of 1 case out of the 104 heretofore reported.[3,4]

In general, the bone metastases appeared to be of hematogenous spread. Case II showed destructive changes in the fourth and seventh ribs. Case IV had osteolytic metastases to the ribs, pelvis, spine, and femur, and what is more unusual, osteoblastic metastasis to a lumbar vertebra (Fig. 5 and 6). Case XII (Fig. 7) was found to have metastatic involvement of the vertebrae, humerus, femur, pelvis, rib, scapula, and clavicle. At postmortem examination of the last 2 cases, all the thoracic and lumbar vertebrae showed on gross inspection a yellowish-white mottling of their bodies, obviously invasion by tumor. The bone lesions were all infiltrative in type and many tended to grow into the adjacent soft tissue.

FIG. 3. Case V. Synovioma of leg. (*A*) Note the deformity of the bone from extrinsic pressure. (*B*) Close inspection of the original lateral roentgenogram at the site of the arrow reveals a break in the cortex and periosteal proliferation.

In the differential roentgenologic diagnosis the following should be considered: myositis ossificans, neurofibroma, fibrosarcoma, and pigmented villonodular synovitis. The last may be eliminated if the mass is outside the joint space. In neurofibroma and fibrosarcoma calcification rarely occurs. The calcification in myositis ossificans tends to follow streaks or tissue planes, which is not the case in synovioma.

It must be recognized that in those cases in which the mass is not in close proximity to a joint, and in the absence of calcification, the diagnosis by roentgen examination depends very much on chance. The preoperative diagnosis in 2 instances of lipoma cannot be explained. Roentgenologically it should have been ruled out because a fat-containing tumor casts a rather characteristic shadow, with the entire mass being of less density than the capsule or adjacent muscle; in other words,

FIG. 4. Case IV. Synovioma within the knee joint space.

it is of a density similar to that of fat elsewhere in the body. A synovioma, on the other hand, when it contains no calcification, casts a shadow the density of fibrous tissue or muscle.

PROGNOSIS

The prognosis in synovioma is more grave than the name implies. The point made by Berger,[2] and others,[3] that a more appropriate and descriptive term would be "synovial sarcoma" is well taken. Both the name and the fact that, as a rule, the tumor is encapsulated and slowly growing tend to mislead one who is unaware of the course of the disease. An accurate diagnosis is of first importance. It may be suspected from the clinical and roentgen findings, but it can be established only by histopathologic examination. Frozen section has not given an accurate diagnosis in most instances; permanent sections and frequently special stains are required. In those cases operated on at this hospital, the short delay attendant upon histopathologic examination of a biopsy specimen has not appeared to seriously affect the prognosis.

Of the 104 cases reported by Haagensen and Stout,[4] only 3 five year cures were found. The material in the present study has been reviewed with the question in mind of prognosis from three approaches: the location of the tumor, the character of the tumor, and the type of treatment the patient received initially (Table 1).

Location of the Tumor. In 8 patients the synovioma was located in the lower extremity about the knee or distal half of the femur. Four of these died in one to four years after the initial treatment; 4 are living without evidence of disease at two and a half, two and three-fourths, three and a half, and sixteen years.

In 5 patients the tumor was situated in the upper extremity. Four of these are dead in periods of from one to twelve years after treatment; 1 is alive and well six and a half years after surgical removal.

The 4 patients in whom the tumor was located elsewhere than in an extremity have all died except one who is alive one and a half years after radical excision of a synovioma in the neck. The other 3 died nine months, three and a half, and four

FIG. 5. Case IV. Osteolytic metastasis to the superior ramus of the pubis.

years respectively after operations on tumors of the chest wall, the axilla, and the groin. Radical excision is not easily carried out in these areas, and, furthermore, due to the location, the tumor is less likely to cause symptoms; the patient may be unaware of its presence until it has involved a structure not readily resectable.

The chief bearing the location of a synovioma has on the prognosis seems to lie in the operative freedom it allows the surgeon. A tumor located in an extremity has the advantage that in most instances it can be radically excised or, if necessary, the part may be amputated.

Character of the Tumor. From the operative notes available in 11 cases, 8 of the tumors were described as encapsulated, 2 were discrete but without capsule and were easily separated from the normal tissue; 1 was infiltrative. The latter was described as being attached to the greater trochanter and was dissected out with considerable difficulty. It is probable that this particular tumor was either highly malignant or that the history of eight months' duration was incorrect, as the majority of synoviomas are encapsulated and slowly growing until the capsule is broken, spontaneously or at operation.

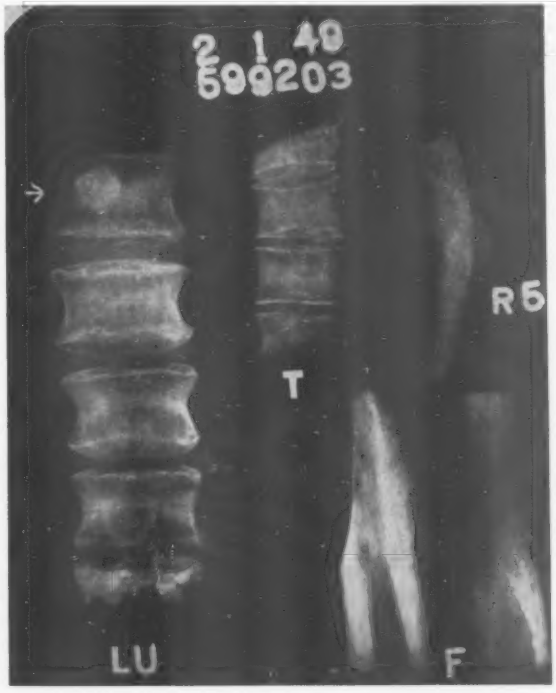

Fig. 6. Case iv. Roentgenogram of postmortem specimens, revealing osteolytic metastases to spine, rib, and femur, and osteoblastic metastasis to a lumbar vertebra.

Fig. 7. Case xii. Osteolytic metastasis to right humerus. A synovioma had been locally excised from the left shoulder nine months before. (Autopsy)

The fact that most of these tumors appear to be encapsulated may well have some bearing on the prognosis. From this limited number of cases it is difficult to draw definite conclusions. Those patients, however, who have done best were in the group in which the tumor was encapsulated.

Initial Treatment. Local *simple excision* was the primary treatment given in 10 cases; in 4, *radical excision* was employed; 2 were *irradiated;* and in 2, *amputation* was performed.

TABLE I

STUDY OF 17 CASES OF SYNOVIOMA TREATED AT THE MASSACHUSETTS GENERAL HOSPITAL

Case	Sex	Age	Location Tumor	Presenting Signs and Symptoms	Duration Symptoms Before 1st Treatment	Preoperative Roentgen Diagnosis
I	F	65	*Knee* medial	Dull ache over smooth nontender, immovable 6×10×12 cm. mass	1 yr.	Soft tissue mass
II‡	M	24	*Knee*	Sensitive spot at side knee. 4 yr. pain, stiffness. 1 yr. tender swelling	6 yr.	Large sharply defined irregular calcified mass
III	F	26	*Knee*	Firm mass behind knee; no pain until 1 mo. before operation when signs of inflammation developed	5 yr.	None taken
IV‡	F	32	*Knee*	Pain and swelling; no mass	3 yr.	Ill-defined prepatellar mass with calcium
V	F	29	*Leg* medial prox. third	Pain and swelling; no definite mass	4 yr.	Pressure deformity of bone; periosteal proliferation
VI	M	18	*Thigh* lower medial	Firm, nontender mass. No pain	3 mo.	Lobulated, soft tissue mass with calcium
VII	M	20	*Thigh* prox. outer	Nontender, firm, fixed 10×6 cm. mass. 5 mo. dull ache	8 mo.	Lobulated mass containing calcium
VIII	F	41	*Thigh*	Pain, numbness and paresthesia	5 mo.	Well circumscribed mass
IX	F	20	*Groin* inguinal canal	Nontender 4 cm. mass in right inguinal canal; occasional pain	2 yr.	None taken
X	F	29	*Arm*	Small nodule; no pain	1 yr.	None taken
XI	F	17	Axilla	Soft tissue swelling with pain	1 yr. 8 mo.	None taken
XII	F	36	*Shoulder*	Pain in shoulder	2 mo.	None taken. Later films showed bone metastasis
XIII	F	46	*Arm* upper third	Swelling, pain, 2 cm. firm, nontender mass above right elbow	1 yr. 10 mo.	None taken
XIV	M	19	*Forearm*	Nontender 19×14×12 cm., slowly growing mass	2 yr. 6 mo.	Lobulated mass with calcium; periosteal proliferation
XV	M	47	*Elbow*	Firm nontender mass	1 yr.	None taken
XVI	M	4	*Chest wall* post.	Pain in back and left shoulder; atrophy left arm	2 mo.	Mass on left chest wall
XVII	M	57	*Neck* post. lat.	Stiffness, intermittent 3 mo. nontender mass	1 yr.	Soft tissue mass

Preoperative Diagnosis	Previous Treatment	Massachusetts General Hospital Treatment	Character of Tumor	Survival after 1st Treatment		
				Alive and Well	Dead (yr./mo.)	Metastases
Fibrosarcoma	None	Simple excision, 1944	Encapsulated		1/0	Pulmonary
Myositis ossificans	Simple excision Nov. 1935 X-radiation Nov. 1936	Amputation Feb. 1937	Discrete		4/0	Pulmonary Bone
Sarcoma	None	Radical excision 1933	Encapsulated	16		—
Ruptured medial meniscus	Removal medial meniscus Feb. 1947	Simple excision Feb. 1948 Radical excision Mar. 1948 Amputation mid-thigh May 1948	Unknown		2/0	Pulmonary Bone (Autopsy)
Ewing's tumor	None	Amputation mid-thigh 1948	Encapsulated	1/3		—
Myositis ossificans	None	Radical excision Mar. 1942 Postoperative x-radiation	Encapsulated	6/3		—
Sarcoma	None	Simple excision Jan. 1938	Infiltrating		2/9	Pulmonary
Fibrosarcoma	None	Radical excision 1946	Encapsulated	3/3		—
Inguinal hernia	Simple excision	Radical excision July 1945 Excision lymph nodes May 1946 X-radiation August 1948	Encapsulated		4/2	Pulmonary
Lipoma	Simple excision	Radical excision Apr. 1943 Disarticulation shoulder July 1943	Unknown	6/2		—
Tuberculous adenitis	Simple excision Jan. 1937 X-radiation	Radical axillary dissection Oct. 1938 X-radiation Dec. 1938	Encapsulated		3/6	Pulmonary
Subdeltoid bursitis	Simple excision	None	Unknown		1/2	Pulmonary Bone (Autopsy)
Tumor	Simple excision Jan. 1943;* postoperative x-radiation	Amputation Oct. 1944	Unknown		2/0	Pulmonary
Sarcoma	Simple excision Sept. 1943†	Amputation Nov. 1944	Encapsulated		5/0	Widespread
Osteogenic sarcoma	X-radiation 1937*	None	Unknown		12/2	Pulmonary (Autopsy)
Lympho-sarcoma	None	X-radiation Nov. 1938 Resection chest wall with postoperative x-radiation Feb. 1939	Unknown		0/9	Pulmonary (Autopsy)
Lipoma	None	Radical excision Aug. 1948	Discrete	1/0		—

* Amputation refused after histopathologic diagnosis.
† Amputation refused after biopsy taken 4 months before excision.
‡ Massachusetts General Hospital Case Record, Case 24321. *New England J. Med.*, 1938, *219*, 204, and Case 35121. *New England J. Med.*, 1949, *240*, 472.

Of the 10 cases in which the synovioma was first excised locally, 1 is alive six and one-fourth years later; 9 are dead. The longest survival was five years, but in this instance, amputation followed in one year and widespread metastases developed during the remaining years of the patient's life.

Radiation therapy was employed as the primary treatment in Case XV and Case

FIG. 8. Case XV. Pulmonary metastases which developed twelve years after radiation treatment to a synovioma of the right elbow. (Autopsy)

XVI. In the former an unknown amount of roentgen radiation was delivered at another hospital after biopsy had proved the nature of the tumor and after the patient had refused amputation. He remained in good health for twelve years, at the end of which time he developed pulmonary metastases and died. The diagnosis was confirmed by postmortem examination. This is the only case suggesting any prolonged benefit from roentgen therapy.

Case XVI was given, with 200 kv., five roentgen treatments at the rate of 300 r (air) per day to the chest wall, with subsequent slight regression in the size of the tumor mass. Two and a half months later, the chest wall was excised and an additional dose of radiation, 2,700 r (air) with the same technical factors, was given. Again the tumor decreased slightly in size, but the patient died within nine months of the first treatment.

In Case VI, roentgen irradiation was given *following radical excision*. The patient received 3,300 r (air) at the rate of 300 r (air) per day, using 1,200 kv. Six years have elapsed since treatment and he has shown no evidence of recurrence.

Six other patients received irradiation to recurrent disease, to a total dose of 3,000 r to 4,000 r (air). None showed dramatic improvement and all died of the disease.

From this limited experience with radiation therapy, it would seem to have relatively little curative value and but slight palliative effect in the treatment of synovioma.

Amputation is probably the treatment most likely to result in cure, but in the majority of cases where it is technically possible, particularly in a young person, this drastic measure will be refused by the patient at the time it is first recommended. In this group, only in Case V was amputation carried out as the initial treatment; the patient is living without evident disease one year and three months postoperative. Three of the group refused amputation. In Case X, local recurrence in the operative site had followed two different simple excisions, and at a third operation, the arm was disarticulated. In the six years since the last operation the patient has shown no evidence of disease.

Of the 8 patients who received primary treatment at this hospital, 2 were treated by simple excision, 4 by radical excision, 1 by amputation, and 1 by roentgen irradiation.

All 4 cases first treated by radical excision are living and apparently free of disease one and one-fourth, three and one-fourth, six and one-fourth, and sixteen years respectively following operation.

From the above implications it would seem that radical excision should be attempted first in cases in which the synovioma is encapsulated. The patient should be kept subsequently under close observation. Amputation might be reserved for

use in the event of local recurrence, which in this group seemed most likely to occur within one year after operation.

SUMMARY AND CONCLUSIONS

Synovioma is not a common tumor. It occurred at the Massachusetts General Hospital in seventeen cases out of 650,000 hospital admissions in the past sixteen years. The sex incidence was ten females to seven males. Synovioma tends to attack the young rather than the old; 60 per cent of the patients were under thirty years of age.

Clinically there is little to identify synovioma from any other neoplastic soft tissue mass.

Roentgenologically certain findings are of diagnostic value; it presents the shadow of a soft tissue mass, whose outline is lobulated, in or near a joint. In some instances, calcium may be present within the mass and, when present, appears as a fine speckling, irregularly arranged. Differential points have been described which may help in distinguishing synovioma from other tumors; in particular, neurofibroma, fibrosarcoma, pigmented villonodular synovitis, lipoma, and myositis ossificans.

In the late stages of the disease, remote metastases are common, particularly in the lungs. An unusual finding is metastases to bone; this was observed in three instances.

The prognosis in synovioma is grave; only three five year cures have been reported in the literature. Of the group presented, four lived five years or more without evidence of disease, one of whom died at the end of twelve years.

The prognosis may well be influenced by the type of treatment instituted when the patient is first seen. Simple excision as the primary treatment was uniformly unsuccessful. Radiation therapy was of real value in only one of the nine to whom it was given; in the others, its beneficial effect was questionable. Amputation or radical excision can be considered the most likely methods of treatment to produce a cure.

In synovioma, as in other malignant tumors, early diagnosis and prompt, judiciously chosen treatment are the factors of utmost importance. Close observation of the patient for many years following treatment is equally vital in order that recurrence or metastases may be recognized and treated, or forestalled.

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APPEARANCE OF CENTERS OF OSSIFICATION IN THE HUMAN PELVIS BEFORE BIRTH

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THE time of onset of ossification of the various portions of the skeleton, and factors which influence and modify the rate and extent of ossification have long attracted interest, as evidenced by the voluminous literature on these subjects. Despite this interest, the prenatal ossification of certain areas, particularly that of the bones of the pelvis, does not appear to have been studied extensively. Undoubtedly one reason for this has been the difficulty in securing an adequate number of specimens.

Standard textbooks of anatomy are not in close agreement on the time of appearance of the centers under discussion. In some texts statements appear to have been repeated from edition to edition and are based on original work which was done many years ago.

It is quite possible to determine the time of earliest ossification by a study of microscopic sections of the areas in question but this is a very laborious procedure. On roentgenograms it is possible to see very small centers of ossification and, even if one has a large series, the effort involved in amassing data is not excessive. Cleared specimens can be used; however, this method does not display centers which would not be seen on a roentgenogram and is time-consuming. It must always be kept in mind that the time of appearance of a center roentgenologically is somewhat later than the actual onset of ossification.

Hess[8] in 1917 reported his findings based on 55 cases. Adair[1] in 1918 reported on a series of 78 individuals, 18 of which were studied from roentgenograms, 25 by dissection, and 35 by observation of cleared specimens. Age was estimated from crown-rump length and sex was stated where it was possible to determine it. Hill[9] in 1939 reported on a roentgenographic study of 543 fetuses of known size, sex, and color. He was primarily interested in the skull and extremities but did give his findings for certain pelvic centers. Flecker[5] in 1942 included in his publication findings on a group of 60 fetuses of known sex and length. Noback[12] in 1944 reported on a series of 40 cases of known crown-rump length but sex was not stated. In the discussion of the individual centers specific reference to the findings of these men will be made.

MATERIAL

The Department of Anatomy has a large collection of roentgenograms of embryos and fetuses of known size, sex, and color. Fetuses having developmental faults such as anencephaly, hydrocephaly, spina bifida, and gross defects of the limbs were rejected. Some of the earlier roentgenograms had to be omitted because of difficulty in interpretation. A total of 640 specimens remained and these have been summarized in Table 1. Many of the specimens studied by Hill are included.

The stated age of gestation is present in the records of each case but this estimation is notoriously unreliable and in many instances is obviously in error. I have divided the specimens into nine groups based on crown-rump length. The groupings are approximately comparable to Arey's[2] table of relation of age and crown-rump length.

The findings will be discussed for each ossification center beginning with the primary elements of the os coxae, followed by a report on the sacral and coccygeal centers.

ILIUM

No primary center of ossification was visible in the two smallest embryos having

a crown-rump length of 32 and 47 mm. respectively. The primary center was seen in every fetus having a crown-rump length of 61 mm. or more. It first appeared as a small area in the region above the acetabulum. This area increased in size rapidly and by the time the fetus had reached a length of 130 mm. the shadow had a characteristic shape with a well visualized iliac blade and a definite greater sciatic notch.

There is a suggestion that the shadow for the greater sciatic notch and for the iliac blade becomes clearly defined a little earlier in the female embryos. Such a finding would be consistent with the known female precocity in later stages of development, but there is no definite proof from the material available for this study that such precocity exists in the early ossification of the ilium.

Of the standard textbooks, Gray[7] and Quain[14] state that this center appears at the eighth or ninth fetal week, Cunningham[4] and Piersol[13] give early in the third fetal month, and the latest edition of Morris[11] gives second fetal month. Hess gives ninth week, Adair the sixtieth to sixty-fifth fetal day (crown-rump 30–35 mm.), Noback sixty-fourth day approximately (crown-rump 38 mm.), Hill states that it must certainly ossify during the second month. Flecker observed this center in a fetus of 32.5 mm. (49 days exact). The evidence indicates that the primary center of ossification for the ilium should be discernible on a roentgenogram of a fetus with a crown-rump length of about 60 mm. There is no evidence of any difference in time of appearance due to sex or color.

ISCHIUM

The primary ossific center for the ischium appears in that portion of the cartilage lying below and behind the acetabulum. It was first observed in a male white fetus of 112 mm. crown-rump length. In the group 81 to 135 mm. it was present in 11 of 31 cases, or in 36 per cent. When these are subdivided into groups of the same sex and color, the findings are 7 (41 per cent) of the male white, 3 (43 per cent) of the female white, none of the male Negro, and 1 of the female Negro. The center was present in every fetus with a crown-rump length of 135 mm. or more.

Cunningham gives the fourth fetal month as the age for the appearance of this center and other standard texts give the third fetal month. Hess gives the sixteenth to seventeenth week, Adair the ninety-fourth to ninety-eighth day, Noback at a crown-rump length of 105 mm. (3.5 lunar months); Flecker saw it in a fetus of 109 mm. (15 weeks) and in all longer ones. Hill states

TABLE I

SUMMARY OF SPECIMENS STUDIED

Crown-Rump Length (in mm.)	Male White	Female White	Male Negro	Female Negro	Total
Under 60					2
61 to 80	2	1	1	1	5
81 to 135	17	7	6	1	31
136 to 159	12	2	7	4	25
160 to 209	32	33	16	16	97
210 to 249	40	28	17	16	101
250 to 279	38	18	17	12	85
280 to 339	61	42	33	25	161
340 or more	59	36	21	17	133
Total	261	167	118	92	640

that the ischium appears during the third or fourth month.

This center should be visible when the fetus attains a crown-rump length of 130–140 mm. It does not appear earlier in the female than in the male.

PUBIS

A primary center of ossification was first observed in the region of the superior ramus in a male white fetus of 156 mm. crown-rump length, and in no other of the group 136 to 159 mm. In the next longer group, 160 to 209 mm., 44 per cent showed a center. In the group 210 to 249 mm., it was present in 88 per cent. It was present in 98 per cent of the individuals in the groups 250 to 279 mm. and 280 to 339 mm. It was present in all individuals of 340 mm. or more. The time of appearance of this center is given by Morris as the fourth month, by Quain, Gray, and Piersol as the fourth or fifth month, and by Cunningham as the fifth or sixth month. Hess gives the twenty-first to twenty-eighth week, Adair the 129th day (crown-rump 150 mm.), Noback at a crown-rump length of 175 mm. (5 lunar months). Flecker first observed this center in a male of 165 mm. (20 weeks) and in a female of 205 mm. (23 weeks).

In Table II is summarized the time of appearance arranged according to sex and color. There is a tendency for this center to appear earlier in the female than in the male. Color is not a factor. There is no evidence in this study that any definite sexual difference in time of appearance of centers of ossification occurs before the sixth lunar month (crown-rump 160 to 209 mm.). This is in agreement with the findings of Hill for the cuboid, lower femoral epiphysis, and proximal tibial epiphysis.

TABLE II

SPECIMENS SHOWING OSSIFICATION OF PRIMARY CENTER FOR PUBIS

Crown-Rump Length (in mm.)	Male White	Female White	Male Negro	Female Negro	Total
136 to 159	1 (0.91%)				
160 to 209	14 (44%)	18 (55%)	4 (25%)	7 (44%)	43 (44%)
210 to 249	32 (80%)	27 (96%)	15 (88%)	15 (94%)	89 (88%)
250 to 279	36 (95%)	18 (100%)	17 (100%)	12 (100%)	83 (98%)
280 to 339	61 (100%)	40 (95%)	33 (100%)	23 (92%)	157 (98%)
340 or more	all show ossification				

The primary center of ossification for the pubis should be present roentgenologically in female fetuses of about 160 mm. crown-rump length and in male fetuses a few millimeters longer.

CENTRA OF SACRAL VERTEBRAE

In Table III are summarized the findings on time of appearance of centers of ossification in the centra of the sacral vertebrae. They appear in order from above downward. The upper three should be present

in a fetus of 80 to 90 mm. crown-rump length. The fourth should be present at about a crown-rump length of 160 mm., and the fifth at 200 mm. The fourth shows some range in time of appearance and the fifth is quite variable, in some cases being still unossified at birth. No such range is seen in the upper centra. No evidence of difference in time of ossification due to sex is seen. Quain, Gray and Morris state that centers for the upper sacral vertebrae appear in the eighth or ninth week and the others appear soon after. Cunningham and Piersol give a somewhat later date. Hess gives the eleventh week for the upper sacral centra, the twelfth week for the lower, and the thirteenth to the twenty-eighth week for the fifth. Noback states that the first sacral centrum appears on the seventy-fourth to seventy-sixth day (crown-rump 51 to 52 mm.) and the others should be present by the 129th day (crown-rump 150 mm.). Noback's article is somewhat confusing on these areas but apparently he found the first and second sacral centra ossified at a crown-rump length of 88 mm., the third at 139 mm., the fourth at 175 mm., and the fifth at 352 mm. Flecker believes that there is a wide variation in the time of appearance of these centers. He saw the first two in a female of 62 mm. (11½ weeks) and all five in a male of 90 mm. (13 weeks).

Table III

SPECIMENS SHOWING OSSIFICATION OF CENTRA OF SACRAL VERTEBRAE

Crown-Rump Length (in mm.)	S_1	S_2	S_3	S_4	S_5
61 to 80	2 (40%)				
81 to 135	31 (100%)	30 (96%)	23 (74%)	5 (16%)	
136 to 159	25 (100%)	25 (100%)	25 (100%)	11 (44%)	2 (8%)
160 to 209	97 (100%)	97 (100%)	97 (100%)	92 (95%)	28 (29%)
210 to 249	101 (100%)	101 (100%)	101 (100%)	101 (100%)	66 (65%)
250 to 279	85 (100%)	85 (100%)	85 (100%)	85 (100%)	68 (80%)
280 to 339	161 (100%)	161 (100%)	161 (100%)	161 (100%)	147 (91%)
340 or more	133 (100%)	133 (100%)	133 (100%)	133 (100%)	128 (97%)

TRANSVERSE PROCESSES OF SACRAL VERTEBRAE

Ossific centers appear in the transverse processes of the first sacral vertebra very soon after the centrum begins to ossify, and centers ossify in the transverse processes of the other sacral vertebrae in order from above downward, usually a little later than the time of onset of ossification in the respective centra. Occasionally os-

sification of the transverse processes of the fourth and fifth sacral vertebrae precedes that of the centra.

Standard textbooks give varying times but the latest editions of Cunningham and Morris agree with the above findings. Hess

TABLE IV

SPECIMENS SHOWING OSSIFICATION OF THE LATERAL MASS OF THE SACRUM

Crown-Rump Length (in mm.)	Number of Ossific Centers Present		
	1	2	3
160 to 209	10 (10%)	1 (1%)	
210 to 249	50 (50%)	9 (9%)	2 (2%)
250 to 279	73 (86%)	32 (38%)	3 (4%)
280 to 339	155 (96%)	127 (79%)	24 (15%)
340 or more	133 (100%)	132 (99%)	50 (38%)

indicates that the transverse processes ossify soon after the centra. Adair states that lateral sacral centers first appear when two or three central centers are present at the eightieth to eighty-second day (crown-rump 65 mm.). Flecker observed the neural arches of the first sacral vertebra earliest in a female of 62 mm. (11½ weeks), the second segment in a male of 147 mm. (18 weeks), the third and fourth in a female of 150 mm. (18½ weeks), and in a male of 165 mm. (20 weeks), and all five in a male of 171 mm. (20½ weeks) and in a female of 205 mm. (23 weeks).

LATERAL SACRAL CENTERS

The standard texts all agree that three pairs of ossific centers appear in the lateral mass of the sacrum before birth. The latest edition of Morris states that these appear between the fifth and seventh fetal months. Most of the other texts give the time of appearance between the sixth and eighth months. Hess observed that these ossific centers for the first and second sacral vertebrae appear between the twenty-ninth and thirty-second fetal weeks. Adair and Noback do not mention them. Flecker states that he found three primary centers on each side. The first pair was seen earliest in a male of 180 mm. (21 weeks) and in a female of 220 mm. (25 weeks). The second pair was first seen in a female of 220 mm. (25 weeks), and in all longer fetuses. The third pair was first seen in a female of 220 mm. (25 weeks) and in a male of 312 mm. (33 weeks).

In Table IV are summarized the findings of the present study. The centers appear in order from above downward. The first pair should be present at a crown-rump length of 210 mm., the second at about 280 mm., and the third at about 340 mm. There is no relation to sex or color.

TABLE V

SPECIMENS SHOWING OSSIFICATION OF FIRST COCCYGEAL VERTEBRA

Crown-Rump Length (in mm.)	
160 to 209	1 (4%)
210 to 219	10 (10%)
250 to 279	8 (9%)
280 to 339	38 (24%)
340 or more	71 (53%)

COCCYGEAL CENTERS

Hess found the first coccygeal center ossified between the thirty-seventh and fortieth weeks; Adair and Noback do not mention it. Flecker first noted it in a female of 262 mm. (30 weeks) and in a male of 296 mm. (33 weeks). The standard texts are not in agreement. Quain and early editions of Gray[6] state that this center should be present at birth; the latest edition of Gray

and the first edition of Cunningham[3] give one to four years; Morris and Piersol state birth or soon after; latest edition of Cunningham states one year.

In Table v are summarized the findings of the present study for ossification of the centrum of the first coccygeal segment. It should be ossified at birth. In three term fetuses a center for the second coccygeal segment was also visible. Centers for the coccygeal cornua were visible on one or both sides in eight term fetuses.

BILATERAL ASYMMETRY OF APPEARANCE OF OSSIFIC CENTERS

In those portions of the pelvic girdle which are paired, ossification was occasionally observed on one side only. This asymmetry in time of onset of ossification was limited to the age group where the particular center might be expected to show commencing ossification; in older age groups both sides were ossified. The asymmetry could not be correlated with left or right, with sex, or with color.

SUMMARY

The roentgenograms of 640 fetuses ranging in crown-rump length from 32 to 472 mm. were examined to determine the status of ossification of the pelvis. The specimens were subdivided into groups in accordance with sex, length, and color.

In Table VI is shown the length of the fetus at onset of ossification in the various portions of the skeleton considered in this report. In every case the length is that at which 50 per cent of the specimens of the group displayed ossification of the center under study.

Male fetuses tend to initiate ossification a little later than female fetuses of the same size in the groups of 160 mm. and over. In fetuses of less than 160 mm. there was no obvious difference between the two sexes.

There was no evidence of any variation of onset of ossification due to color.

TABLE VI

Center	Crown-Rump Length
Ilium	60 mm.
Ischium	130–140 mm.
Pubis	160 mm.
Upper three sacral centra	80–90 mm.
Fourth sacral centrum	160 mm.
Fifth sacral centrum	200 mm.
Transverse processes of sacral vertebrae	Soon after respective centra
First lateral sacral center	210 mm.
Second lateral sacral center	280 mm.
Third lateral sacral center	340 mm.
First coccygeal center	Birth

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GROWTH OF THE SHAFT OF THE HUMAN RADIUS AND ULNA DURING THE FIRST TWO YEARS OF LIFE

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A REQUEST for information on the rate of growth of the human radius and ulna in infancy was made by clinical colleagues. An extensive survey of the literature did not give a satisfactory answer. Hence this report on the growth of the shaft of the radius and ulna.

Bakwin and Bakwin (1935) studied the growth of the radius and ulna during the first year of life from serial roentgenograms. In their report they definitely admitted that because of the small number of cases (266 normal films for all the 8 age groups), they were obliged to combine and average the data of both sexes.

Maresh and Deming (1939) studied the rate of growth of long bones (including radius and ulna) in 80 children by anthropometry and by measurement of the shaft from repeated roentgenograms. This study covered the period of early infancy up to the age of six months, only 20 out of the 80 children were measured at the age of twenty-four weeks. Since no sex difference was observed by the authors in this group, the data on boys and girls were combined and averaged.

Though their data suggest certain agreement in the rates of growth as studied by the two methods, Maresh and Deming believe that the roentgen method of measuring is definitely more reliable because "There is so much error inherent in the anthropometric method." Francis (1939), in his comparative study of the growth of the tibia concluded that "The rate of growth obtained by the two methods was comparable and there is no evidence that the roentgenographic method was superior."

In 1943 Maresh alone reported on the growth of major bones in healthy children from early infancy to the age of twelve years. Measurements in the first two years included only 18 boys and 24 girls; the age groups were widely and irregularly scattered between one month and two years. Maresh never pretended that her data for this age were adequate since she states "The numbers of subjects at this early age are too few to permit generalization regarding the entire group, and further work is necessary." For the same reason she also combined and averaged the data on boys and on girls although she detected few sex differences in growth of bones in this group.

In her monograph on "Physical Growth and Development of the Child" based on the study of the Brush Foundation material Simmons reported the average growth of the whole forearm from two to seventeen years by the anthropometric method. Her study does not include measurements of the forearm before the second birthday.

It is superfluous to say that sex differences in growth rate of long bones have been definitely established. Todd (1937) concluded that "not long after children are able to sit up alone the difference in the skeletal developmental level of the two sexes becomes significant." Francis (1939) and Stuart and Dwinell (1942) reported definite sex difference in the length of the tibia. Consequently, to have an accurate knowledge of the growth of any long bone, its length must be studied separately in each sex.

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TABLE I

Age	Number of Cases	Average Length mm.	Range		Average Increase	Average Growth per Month mm. (calculated)
			Shortest mm.	Longest mm.		
		White Male				
		RADIUS				
3 mo.	100	65.90	58	73		
6 mo.	100	73.10	66	81	7.20	2.40
9 mo.	100	80.01	73	90	6.91	2.30
12 mo.	100	85.72	75.5	95	5.71	1.90
18 mo.	100	94.84	84	107	9.02	1.50
24 mo.	100	102.37	95	115.5	7.63	1.27
		ULNA				
3 mo.	100	73.55	65	82.5		
6 mo.	100	81.03	73	90.5	7.48	2.49
9 mo.	100	88.20	80	98	7.17	2.39
12 mo.	100	94.84	85	104.5	6.60	2.21
18 mo.	100	104.99	93	115	10.15	1.69
24 mo.	100	112.64	102	125	7.65	1.28
		White Female				
		RADIUS				
3 mo.	100	62.85	54	70		
6 mo.	100	69.73	60	78	6.88	2.29
9 mo.	100	76.18	66.5	84	6.46	2.15
12 mo.	100	81.73	71	91	5.55	1.85
18 mo.	100	91.70	82	103	9.97	1.66
24 mo.	100	99.44	88	112	7.74	1.29
		ULNA				
3 mo.	100	70.58	61	80		
6 mo.	100	77.67	69	87	7.09	2.36
9 mo.	100	84.70	75	93	7.03	2.34
12 mo.	100	90.73	80	102	6.03	2.01
18 mo.	100	101.62	90	115	10.89	1.81
24 mo.	100	109.79	97	124	8.17	1.36

MATERIAL

The immense material of the Brush Foundation, Western Reserve University, was the source of the data in this report. Serial roentgenograms of the forearm of healthy white children only were used. The left forearm of the child was pronated and firmly applied on the cassette and a focus-film distance of 3 feet was kept constant. Films were selected only when taken within five days before or five days after each specified age. Hazy films with no sharp outline of the bones were discarded. One hundred films were studied for each age group in each sex—1,200 films and 2,400 measurements in all.

The shafts of the radius and ulna were measured in the simplest possible way. The distance from the proximal end to the distal end of the shadow of the shaft was determined to the nearest 0.5 mm. with a "Flower craniometer."

DISCUSSION

In Table 1 the findings are summarized. A study of this table shows that the shafts of the radius and ulna in the male are consistently longer than in the female of

the same age. The average rate of growth per month—as calculated—decreases consistently with increasing age. During the first post-natal year the average increase in length of the radius and ulna is greater in the male; during the second year the average increase is greater in the female.

SUMMARY

The shafts of the left radius and left ulna were measured from serial roentgenograms of healthy white children of each sex at the ages of three, nine, twelve, eighteen and twenty-four months. The length of the shaft of each bone in boys and in girls at these age periods was averaged separately and recorded.

The average length of the shafts of the two bones in boys is consistently greater than in girls of the same age.

The rate of growth of the shafts of the radius and ulna is greater in boys during the first year and is greater in girls during the second year.

The average rate of growth per month—as calculated—of each bone in each sex is almost identical. It diminishes gradually with age in conformity with the general growth of the child.

I wish to express my gratitude: to Dr. Normand L. Hoerr, Professor of Anatomy, Western Reserve University, and to the Brush Foundation for the use of the material included in this study; to Dr. Carl C. Francis for his great help and valuable suggestions and criticism; and to Dr. S. Idell Pyle for her kind interest and assistance.

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DOSE DISTRIBUTION MEASUREMENTS WITH THE UNIVERSITY OF ILLINOIS 25 MEV. MEDICAL BETATRON*

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THERAPEUTIC treatment of patients with the University of Illinois medical betatron was started in August, 1949, and animal irradiation in June, 1949. Prior to these treatments a conventional betatron was adapted for medical treatment and research by the construction of specially designed shielding, beam definition and location equipment, and control and dose measuring apparatus. Extensive measurements were also made on the various dose distributions obtainable with different field sizes and at different skin-target distances. A preliminary report on these techniques and measurements was submitted to *Science*[7] before biological tests began.

A schematic diagram is shown in Figure 1 of the arrangement of the components of the betatron which shaped the roentgen-ray beam and measured its intensity. The collimators were made with different size apertures and were rapidly and accurately interchangeable for different field sizes. In conjunction with each collimator, a corresponding lead insert was located in the portable lead shield. It is to be especially noted that the roentgen-ray beam is actually defined by the collimator and not by the insert. The total shielding resulted in a maximum intensity of radiation outside the beam of one-tenth of 1 per cent of the intensity in the beam.

At these energies the intensity distribution of the roentgen rays is very pronounced in the forward direction; i.e., the intensity drops off to half its maximum intensity at about 4 degrees. As a consequence, differential filtration was necessary to obtain flat isodose surfaces. As indicated in an earlier paper,[8] a low atomic number material is preferable for this because of its relatively small absorption of the higher energy component of the continuous roentgen-ray spectrum. This is in contrast to the dependence of absorption on atomic number with low energy roentgen rays. Conical ensembles of both fiber and aluminum disks have been used effectively as filters. For the larger fields, the use of almuinum permits a more compact filter than carbon or fiber filters, which become objectionably large. Since the smaller diameter fields require less filtration for flat isodose surfaces, it is advantageous to use a different filter with each size of field in order to obtain the maximum intensity. Output intensities ranging from 200 roentgens per minute with the 1 cm. diameter field down to 100 r per minute with the 15 cm. diameter fields (at 80 cm. skin-target distance) were normally employed.

The requirement that both the collimator and insert be changed for a change in field size required more shop work in the construction of additional collimators of different sizes and matching filters. This was justified by the decreased neutron and electron flux in the beam, and the additional output obtained for the smaller fields. Neutrons are produced in the nuclear interactions of high energy roentgen rays

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with all elements. Since 25 mev. is above the threshold for disintegration by neutron ejection for practically all elements, neutrons will surround all betatrons during operation. The flux of neutrons in number per square centimeter-second has been measured in the neighborhood of our betatron in both the slow (<0.1 electron volt) and fast (10-10^7 electron volt) neutron energy regions. The methods of measurement utilized the neutron-induced radioactivity in rhodium foils, and also the detection of neutrons by proportional counters filled with boron trifluoride. These measurements will be described in detail in a separate paper, but it was determined that the flux was sufficiently small that no danger to the patient was involved. It was noted that when the largest collimator was left in position and smaller field sizes obtained by changing the lead insert only (see Fig. 1), the neutron flux doubled in decreasing the field size from 15 cm. to 1 cm. This was because of the greater amount of lead in the path of the roentgen-ray beam. However, when the corresponding collimators were used with the inserts, the neutron flux decreased by about 30 per cent over the same range of field sizes. This was because the collimator was now the source of neutrons rather than the insert, and both the greater distance of the collimator from the patient and the scattering in the insert now combined to decrease the actual neutron flux to which the patient was exposed. These considerations were felt to justify the additional work involved in defining the beam with the collimator rather than with the insert. In this connection it should be pointed out that the neutron flux increases with the atomic number of the filter material which is a further reason in addition to absorption characteristics for using a filter with as low

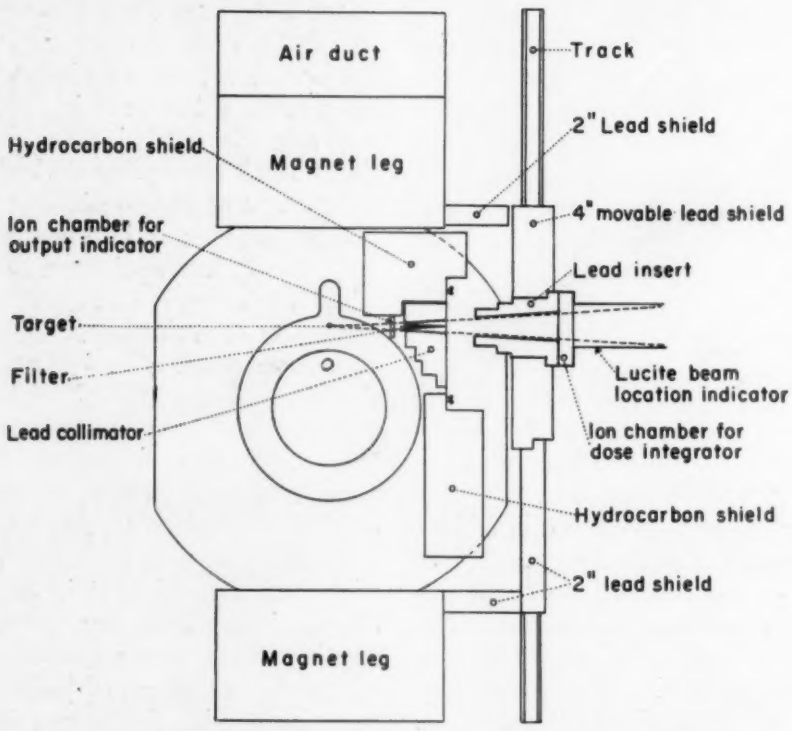

FIG. 1. Schematic horizontal cross-section of 25 mev. betatron.

Fig. 2. Front view of betatron with movable lead shield in position for treatment. The end of the lucite cylinder indicates the diameter and location of the beam for the entrance field on the patient. The mechanical pointer indicates the center of the exit field. A light spot (not shown) is also used to locate the exit field.

an atomic number as possible.

As shown in Figure 1, a small ion chamber is mounted close to the donut as an indicating monitor. In this position the chamber is exposed to a large flux of electrons from the donut which produce most of the ionization in the chamber, rather than the roentgen rays whose flux it is desired to measure. Accordingly, slight changes in magnetic field amplitude, temperature, and alignment prevent a chamber in this position from responding linearly to changes in roentgen-ray flux. This chamber was used, however, as a tuning indicator.

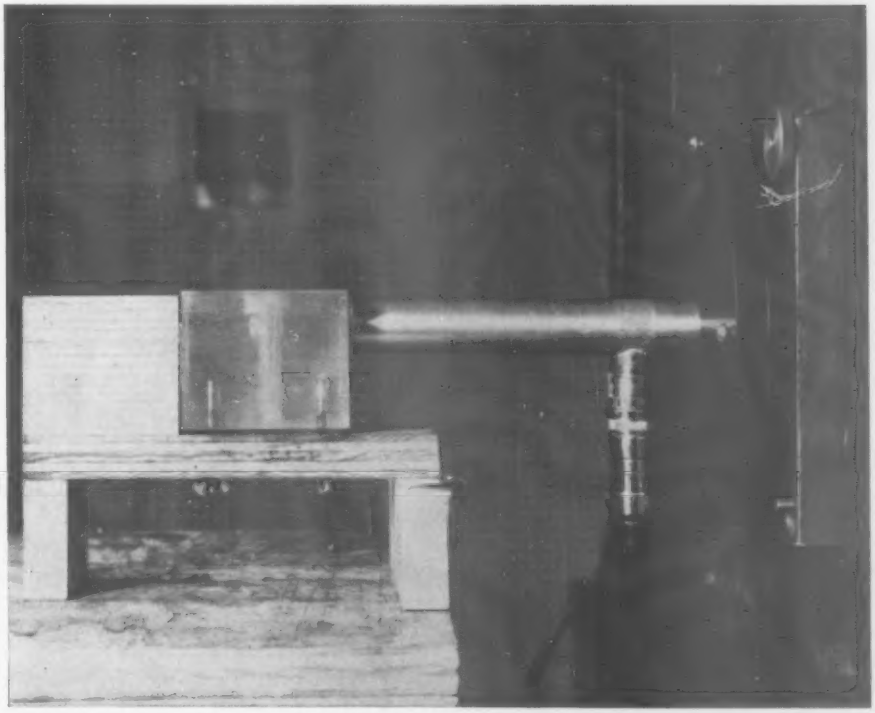

Fig. 3. Side view of sealed ion chamber used with 1 cm. diameter roentgen-ray beam. Lucite block served as holder for rat legs and insured maximum dose at knee joint. Dental films in slots check alignment.

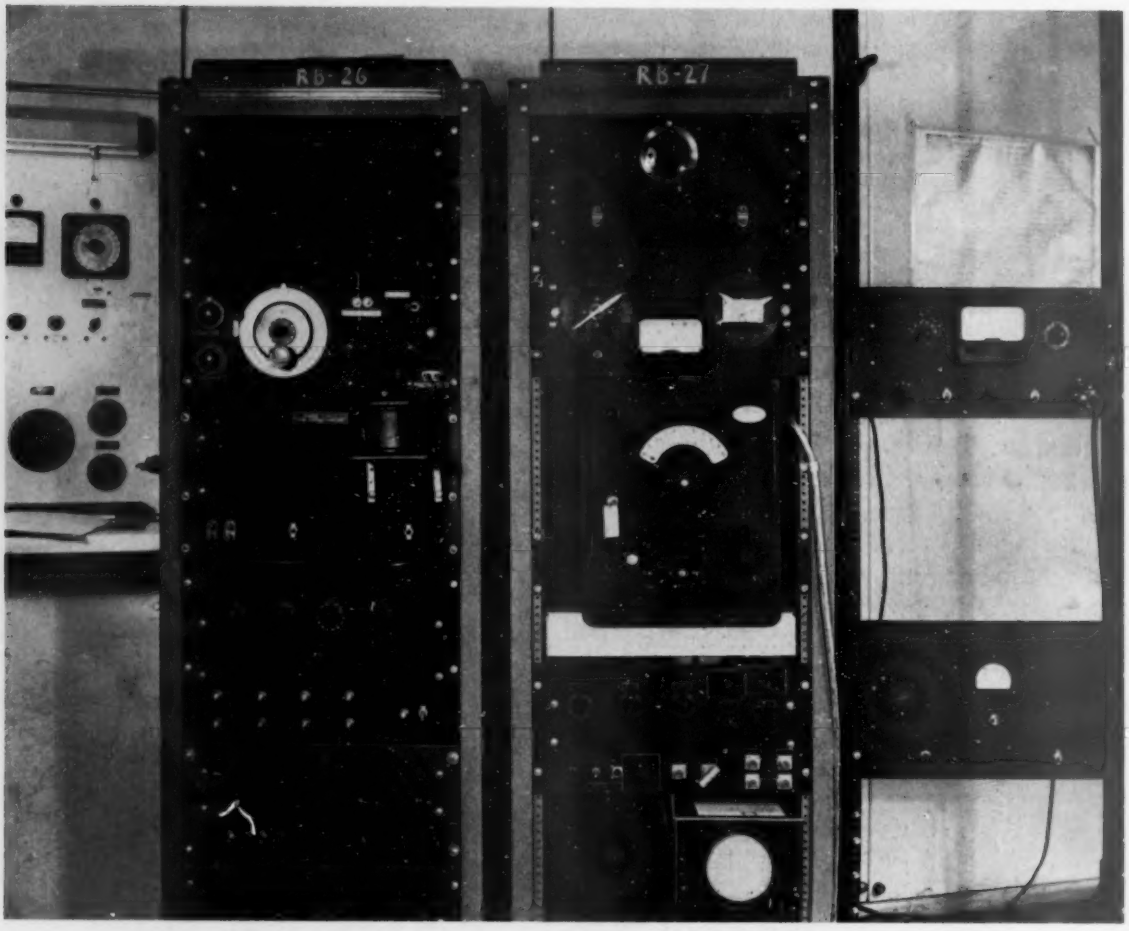

FIG. 4. Control apparatus for the betatron. Left panel contains commercial controls and additional sensitivity selector for integrating ion chamber output. The next panel (relay rack) contains circuits for precise control of maximum roentgen-ray energy, and electron beam extraction circuits. The next two panels on the right contain selsyn motor controls and ion chamber position indicators and D.C. amplifiers and associated circuits.

An additional sealed ion chamber was placed as shown at the end of the insert. Because of the collimation arrangement this chamber was not exposed to electrons, and its response was linear with the roentgen-ray flux. The current from this chamber was amplified in a special pre-amplifier whose sensitivity could be switched from one setting to another, depending on the field size used. The output of this pre-amplifier was fed into the commercial exposure integrating circuit, and controlled and measured the exposure of each treatment of the patients.

In Figure 2 the portable lead shield is shown in position for treatment. The outer end of the lead insert and integrating ion chamber are visible, together with a lucite cylinder which indicates the location and diameter of the beam at 80 cm. skin-target distance. In order to minimize the exit dose, no skin-target distances of greater than 80 cm. are employed. A separate lucite cylinder of appropriate size was used with each different insert. The position of the center of the exit field was indicated both mechanically, as shown, and also with a light pointer. Figure 3 shows the special ion chamber used for the 1 cm. diameter beam.

Some of the circuits used to control and measure the output are shown in Figure 4. These will be referred to later.

The dose measurements were made extensively with both ion chamber and film techniques and have been described briefly elsewhere.[7] The ion chamber measurements were made in the water phantom, which is shown in Figure 5. The front of this phantom contained a window of taut nylon sheet 0.006 inch thick and 16 cm. in diameter. The position of the ion chamber in the water phantom was remotely controlled by means of selsyn motors from the control room. Two selsyn motors are visible on top of the phantom in Figure 5. At the top of the center relay rack in Figure 4 are the indicators which both control and indicate the position of the ion chamber. The direct-current amplifier used initially has been described.[7] Results have also been checked with a special Beckman amplifier and with a modified adaptation of the circuit described by H. E. Johns *et al.*[4] Both flat and cylindrical ion chambers were employed. The wall of the cylindrical chambers consisted of red bakelite (phenol formaldehyde resin) coated on the inside with aquadag. The center collecting electrode consisted of a fine aluminum rod. The inner diameter was 4 mm. and the chamber height was 6 mm. The 10 cm. rod supporting the chamber consisted of polystyrene surrounding the inner conductor in a thin aluminum sleeve. This unit plugged into the pre-amplifier which is visible above the phantom in Figure 5. The front surface of the flat ion chamber consisted of nylon sheet coated on the inside with aquadag. This chamber had an inside depth of about 2 mm. The collecting electrode was a thin carbon disk 5 mm. in diameter. This chamber was used only for depth dose measurements. A sufficiently high potential (150 volts) was employed to collect all ions formed. A typical plot displaying the linearity of response of one of these chambers is shown in Figure 6. A comparison of the response of the flat and cylindrical

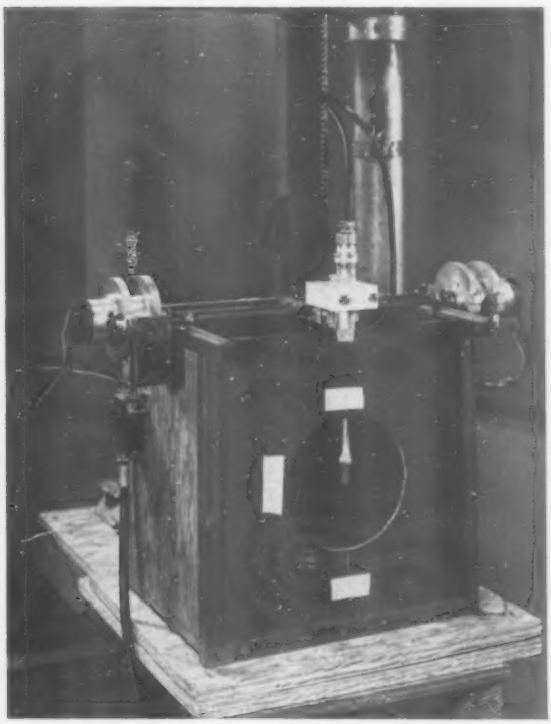

Fig. 5. View of water phantom. Selsyn motors are partially shown, which permit position of the ion chamber to be accurately controlled from the control room. Pre-amplifier stage is visible above phantom below which ion chamber is mounted.

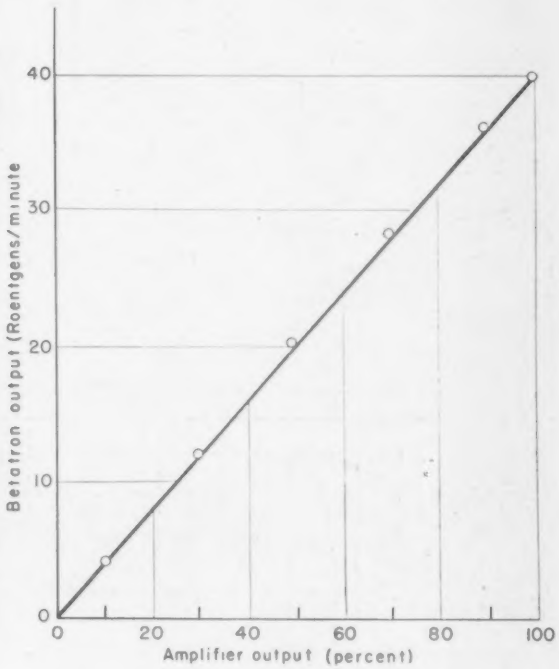

Fig. 6. Linearity of response of the small ion chamber as function of intensity of ionization.

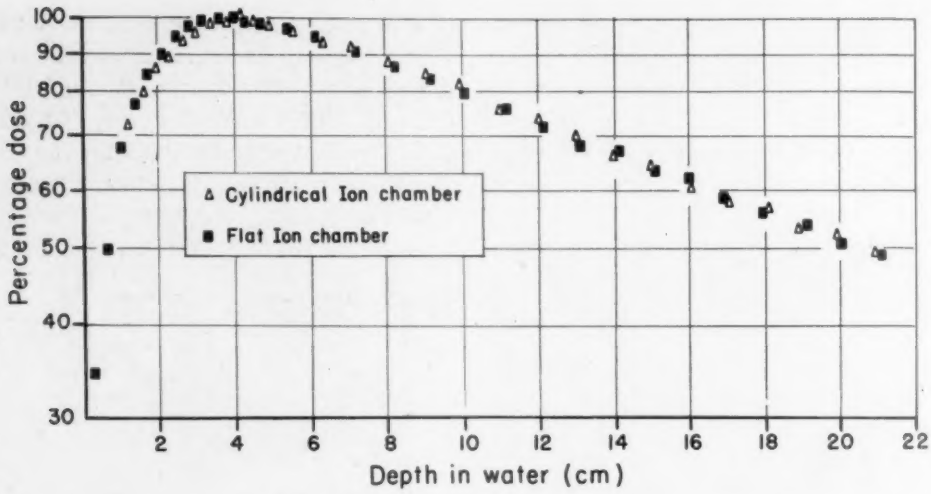

FIG. 7. Comparison of response of small flat and cylindrical ion chambers exposed in water phantom under same conditions.

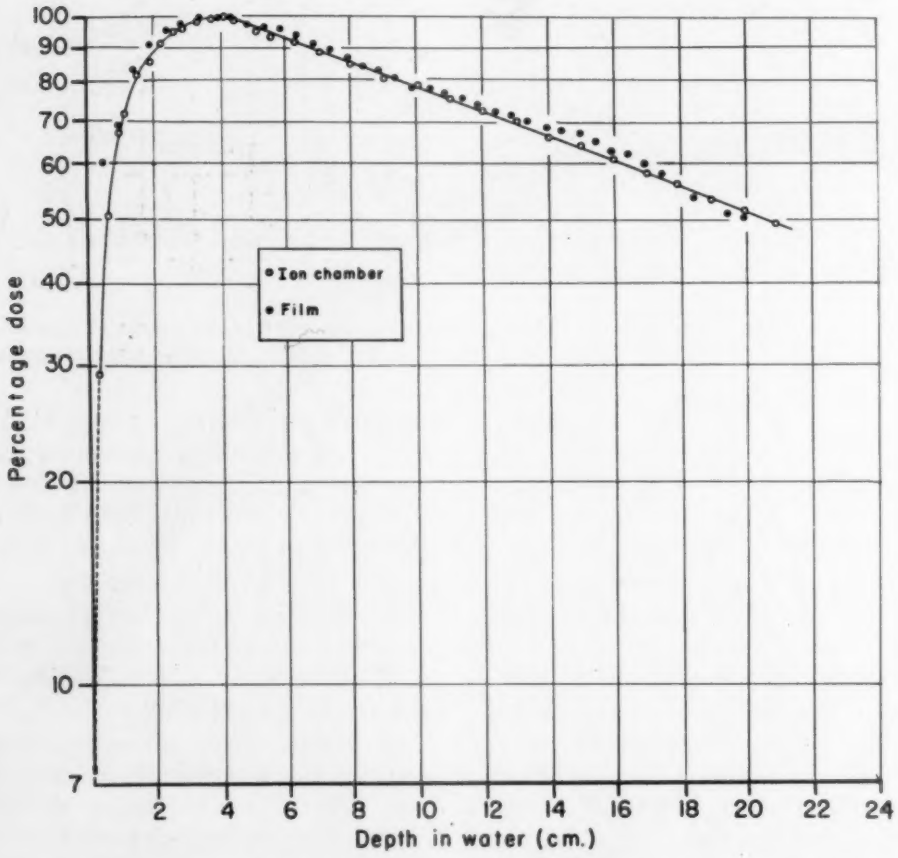

FIG. 8. Comparison of depth dose measurements obtained with ionization chambers and with films in water phantom 2.5 cm. diameter field size at 80 cm. skin-target distance.

chambers is shown in Figure 7, in which the plots are normalized at 100 per cent. Readings were accurate and reproducible to within 1 per cent.

A dummy chamber with no air cavity was employed in tests of the probe. No significant ionization was detected with this dummy chamber in the beam which established that all ionization recorded with the small ion chambers occurred in the chamber cavity.

TABLE I

DEPTH DOSE DATA AT 80 CM. SKIN TARGET DISTANCE WITH ALUMINUM FILTERS

Depth in Water (cm.)	Diameter of Field				
	1.0 cm.	2.5 cm.	5.0 cm.	10.0 cm.	15.0 cm.
0.5	62.5	39.5	42.0	49.0	50.0
1.0	79.0	67.0	68.0	72.5	71.5
2.0	96.5	86.5	88.0	90.0	90.0
3	100.0	96.5	97.5	96.5	98.5
4	98.0	100.0	100.0	100.0	100.0
5	95.0	97.5	98.0	98.0	98.5
6	91.5	93.0	95.0	95.5	96.0
7	88.0	89.0	91.0	92.0	92.0
8	84.0	85.5	88.5	88.5	88.5
9	80.5	82.0	84.0	85.0	85.0
10	76.5	78.0	80.0	81.5	81.5
11	73.0	75.0	77.0	78.5	78.0
12	69.0	72.0	73.5	75.0	75.0
13	66.0	68.5	70.5	72.0	72.0
14	63.0	66.0	67.5	69.0	69.0
15	60.0	63.0	64.0	66.5	66.5
16	57.0	60.0	61.5	63.5	63.5
17	54.0	57.5	59.0	61.0	61.0
18	51.5	55.0	56.5	58.5	59.0
19	49.2	53.0	54.0	56.0	56.0
20	47.0	50.5	51.5	54.0	54.0
21	44.5	48.0	49.5	51.5	52.0
22	42.5				
23	40.5				

Photographic films were also used extensively for relative dose measurements. Industrial type A was used primarily, and with careful handling gave accurately reproducible results. This involved thorough stirring of developer and fixer, constant agitation of immersed films, temperature control of developer, and simultaneous development and fixing of all films to be compared. The densities were measured with an electronic densitometer comprising of photocell, regulated light source, and a stable amplifier. A 2 mm. diameter circular

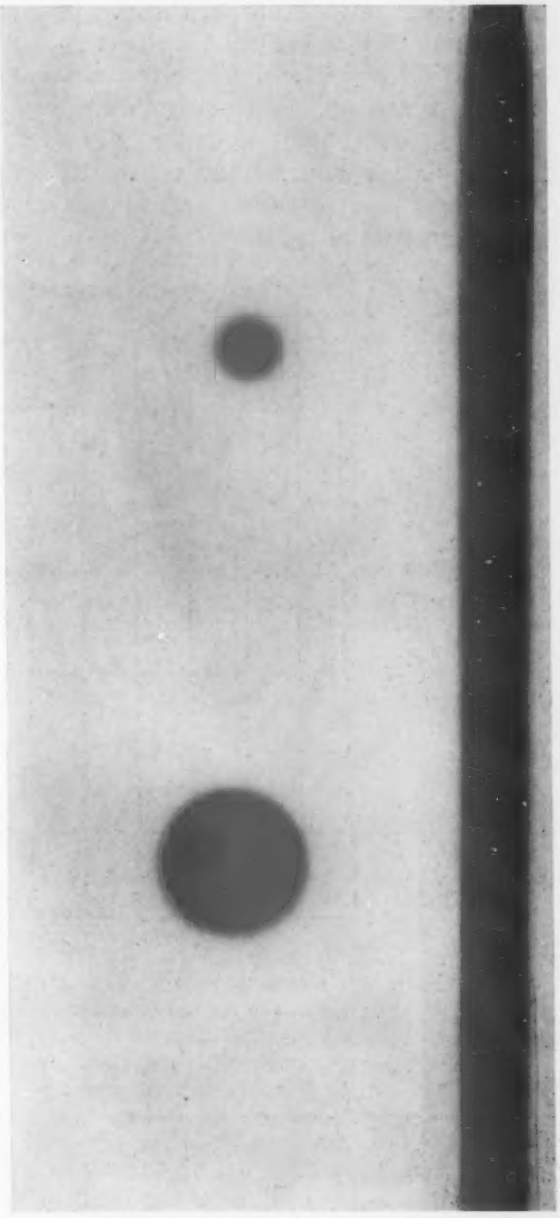

FIG. 9. Films exposed to roentgen-ray beam from the betatron. The long strip was exposed parallel to a 1 cm. diameter beam in water and the small circle perpendicular to the 1 cm. diameter beam 3 cm. deep in pressdwood. Scratch marks in strip are alignment marks. Large circle resulted from exposure perpendicular to 2.5 cm. diameter beam at 4 cm. deep in pressdwood.

area was examined for each density measurement. A pressdwood phantom, in which film strips and Victoreen thimbles could be exposed alternately in the same location, was employed and it was determined that a linear relation[7] existed between the roentgen dose and film density up to densities of nearly 5.

near the surface was consistently about 7 per cent of the maximum dose. Pressdwood sheets were arranged parallel to the beam in the phantom for film studies of the depth dose dependence. It was also found possible to conveniently immerse film strips parallel to the beam in the water phantom. The treatment room is light tight, and re-

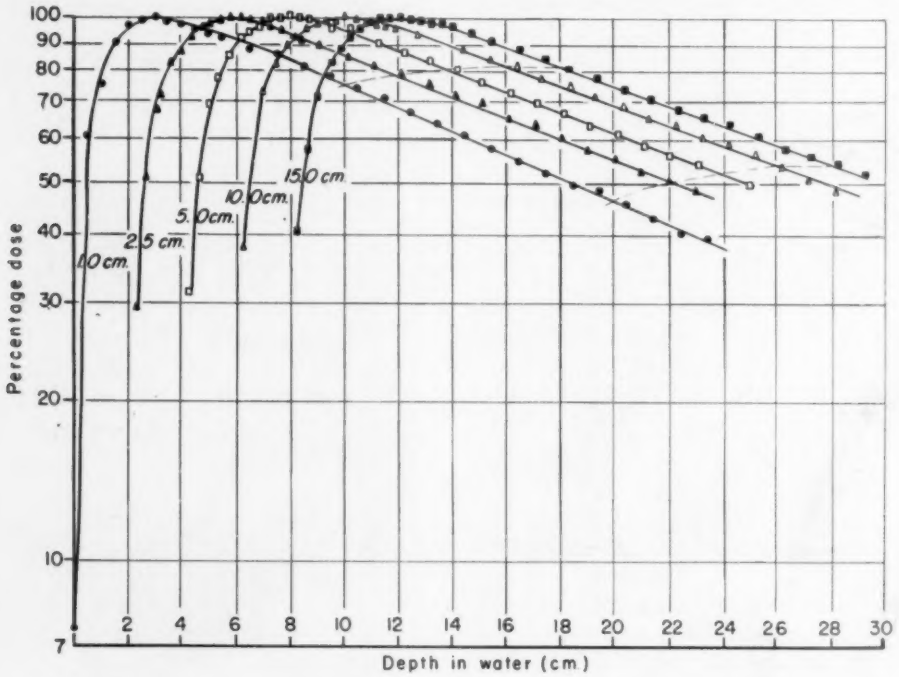

FIG. 10. Depth dose data at 80 cm. skin-target distance taken with different field sizes. All data are ion chamber data except those for the 1 cm. field which were taken with films exposed in the water phantom. All plots are normalized to 100 per cent at depth of maximum dose and all plots are successively displaced by 2 cm. to prevent superimposition of data. Dashed curves indicate dependence of depth dose on field size.

Different phantom arrangements were used in exposures of film to the beam. For checking the isodose surfaces obtained with the ion chambers and for detailed study of the discontinuous dose distribution along the geometrical shadow, pressdwood sheets were arranged perpendicular to the path of the beam in a light-tight box. The films were sandwiched between the pressdwood (density 1.02), and the beam passed through only one thickness of black paper before reaching the first film. In approximately twenty phantom exposures, the relative dose indicated by this film

producible depth dose distributions were obtained with film in this manner also. In Figure 8 the depth dose distributions obtained with an ion chamber and films immersed in the same water phantom are plotted for comparison. In both cases the roentgen-ray beam was 2.5 cm. in diameter at 80 cm. skin-target distance. Film exposures were of particular value for exploratory work and detailed study of regions of steep gradients, but ion chamber measurements were more accurate and more easily reproducible. A film exposed in a water phantom to a 1 cm. diameter beam

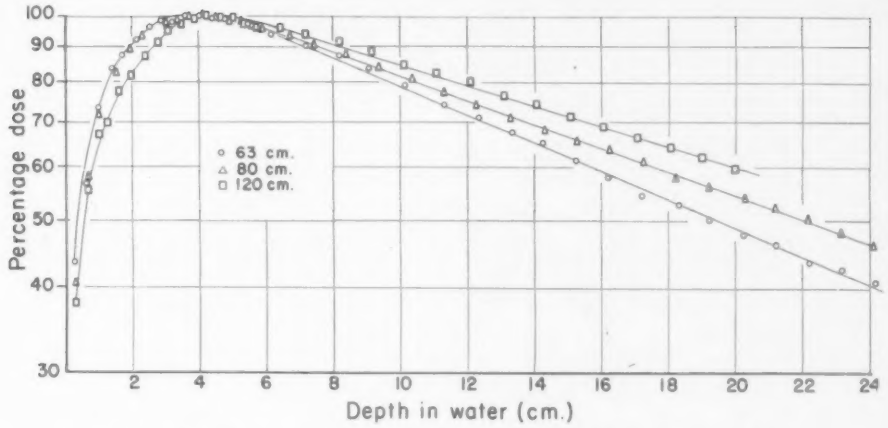

FIG. 11. Depth dose data obtained with large fields at indicated skin target distances.

is displayed in Figure 9. Although the density variation in the original has not been reproduced, some of the discontinuity along the geometrical edge is apparent both in the lengthwise exposure and in the cross-section exposure taken at 3 cm. depth. The larger circle is a cross section film taken at 4 cm. depth with the 2.5 cm. diameter (80 cm. skin-target distance) beam.

In Figure 10 the depth dose distance measurements for different field sizes at 80 cm. skin-target distance are displayed.

TABLE II

UNIVERSAL DEPTH DOSE FOR LARGE AND SMALL FIELDS

Skin Target Distance Field diameter	63 cm. 11.8 cm.	80 cm. 15 cm.	120 cm. 15 cm.	Average for Large Fields	80 cm. 1 cm.
Depth in Water (cm.)					
0.5	44.9	45.8	44.0	44.9	58.8
1.0	66.5	66.3	62.5	65.0	75.0
2.0	85.5	85.5	79.6	83.5	94.0
3	95.0	96.0	92.7	94.6	100.0
4	100.0	100.0	100.0	100.0	100.0
5	100.0	100.0	100.0	100.0	99.8
6	100.0	100.0	100.0	100.0	98.5
7	100.0	98.7	99.3	99.3	96.8
8	97.3	96.5	99.0	97.6	94.2
9	95.4	95.5	96.1	95.7	92.7
10	94.0	94.0	94.0	94.0	90.5
11	92.0	91.5	93.0	92.2	87.7
12	89.9	90.2	91.1	90.4	85.0
13	87.3	88.0	88.5	87.9	82.6
14	85.7	86.5	87.1	86.4	80.7
15	85.0	84.7	85.6	85.1	78.3
16	82.7	82.6	83.5	82.9	76.0
17	80.1	81.2	81.8	81.0	73.5
18	79.0	80.3	80.6	79.9	71.8
19	76.7	77.9	78.8	77.8	70.2
20	75.0	76.7	76.8	76.2	68.5
21	73.0	74.9	75.5	74.5	65.8
22	71.5			71.5	64.3
23	70.0			70.0	62.5

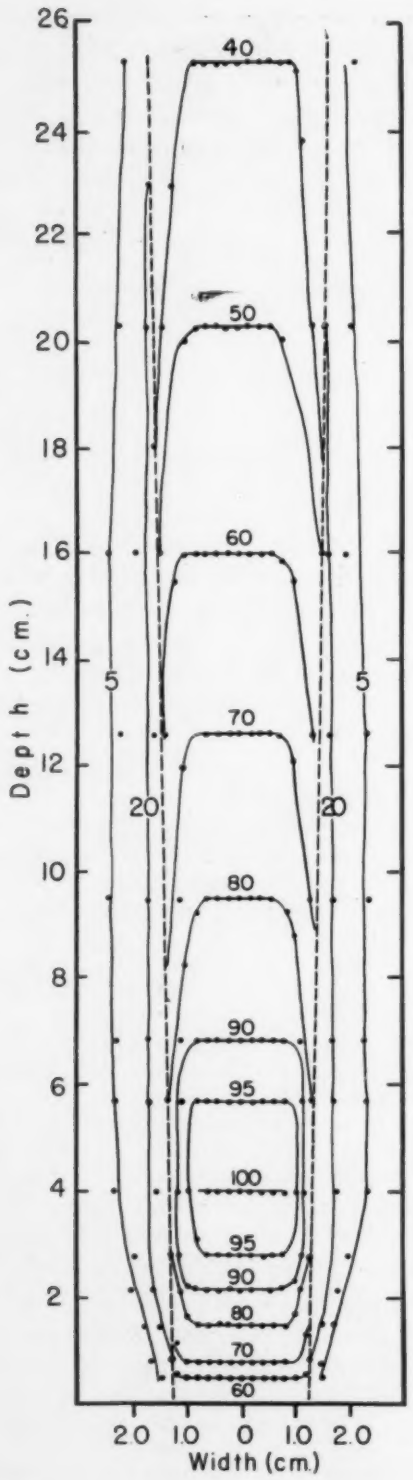

FIG. 12. Isodose distribution measured with films for 2.5 cm. diameter field at 80 cm. skin-target distance.

Each succeeding field size plot has been displaced 2 cm. from the preceding one to avoid superimposition and confusion of plots in the region of the maximum dose. All percentages are relative to 100 per cent taken at the maximum. Though with all the larger field sizes the maximum dose is reached between 4 and 4.5 cm., with the 1 cm. diameter field size the maximum was reached at about 3 cm. depth. Aluminum disks were used for the filter in all of these measurements. The 2.5 cm., 5 cm., 10 cm., and 15 cm. diameter field measurements were made with the small ion chambers already described, while the 1 cm. diameter field measurement was made with film exposed in the water phantom. The results are tabulated in 1 cm. intervals in Table 1. Since the distribution of recoil electrons in the scattering of high energy quanta is more pronounced in the forward direction than with lower energies, the dependence of depth dose distribution on field size would be expected to be less. The dependence of depth dose on field size at lower energies has been demonstrated in many measurements.[1,9] An examination of Table 1 and Figure 10 reveals also a definite dependence of depth dose for field sizes less than 10 cm. diameter. This dependence, however, is small compared with that at lower voltages, and is not as important from the standpoint of practical use. These distributions are in essential agreement with those of Koch, Kerst and Morrison,[6] and with those of Charlton and Breed,[3] as represented by the plot with a copper filter in their Figure 18, and also with those of H. E. Johns *et al.*,[5] with the exception of the limited dependence of depth dose on field size.

In order to ascertain the effect of varying skin-target distance, depth dose distributions were determined at 63 cm., 80 cm., and 120 cm. with large field sizes. These measurements, made in the water phantom with an ion chamber, appear in Figure 11. In Table 11 these data appear with the effect of inverse square law intensity de-

crease removed. This is a reasonable assumption since the target (0.010 inch thick) is effectively a point source and has been experimentally verified. It is seen that the data show close agreement on this basis. The corresponding values for a 1 cm. diameter beam are tabulated in column 6. For field sizes greater than 10 cm. diameter, it appears that the average values in column 5 would constitute a universal depth dose curve for 25 mev. roentgen-ray radiation. Though the actual maximum dose occurs a little beyond 4 cm., for convenience these data have been analyzed on the basis of maximum dose at 4 cm. Consequently, the actual percentage dose at any depth and any skin-target distance for large field sizes would be obtained by multiplying the appropriate value in column 4 by $\left(\frac{S+4}{S+d}\right)^2$ where S is the skin target distance and d is the depth below the surface.

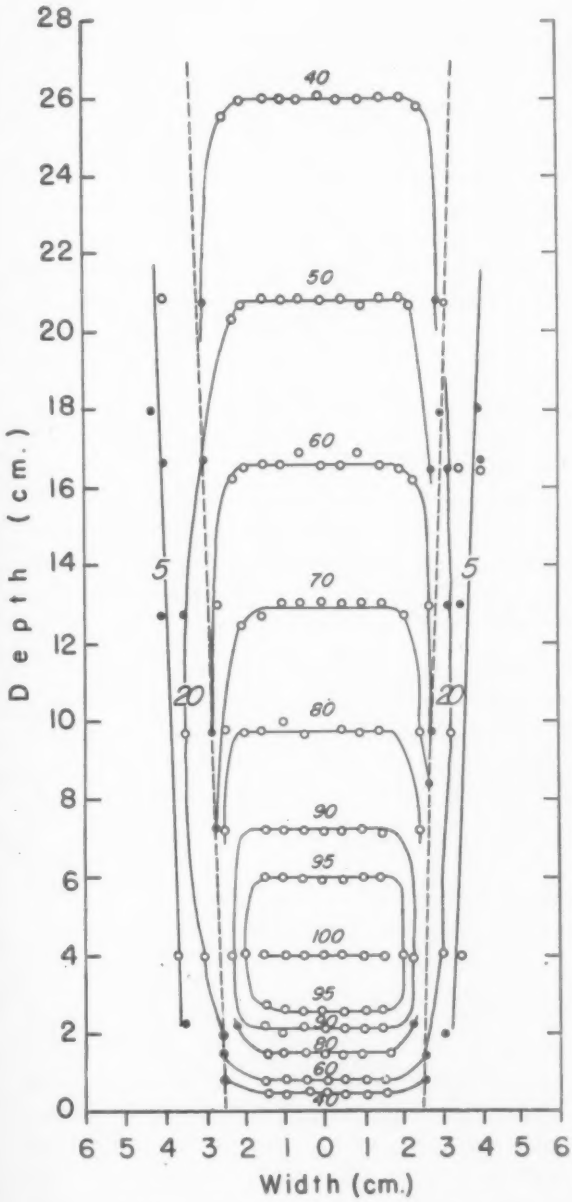

FIG. 13. Isodose distribution for 5.0 cm. diameter field at 80 cm. skin-target distance. Open circles represent ionization chamber data and solid circles represent film data.

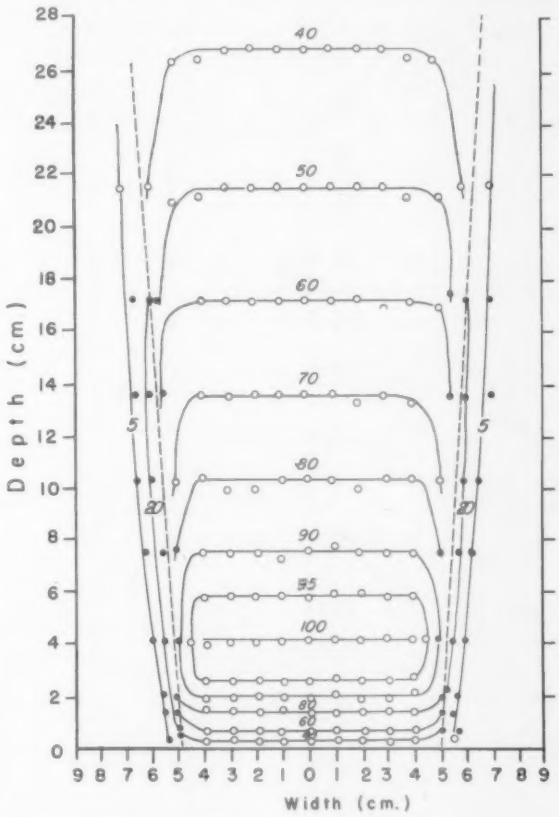

FIG. 14. Isodose distribution for 10.0 cm. diameter field at 80 cm. skin-target distance. Open circles represent ionization chamber data and solid circles represent film data.

For calculations of integral dose and for calculation of resultant dose distributions obtained in the combination of many fields,

it is convenient to represent the dose at any depth D_d as the difference between two exponentials, one governed by the absorption coefficient μ of the primary beam, and the other governed by μ_s, an effective absorption coefficient for the secondary radiation. The representation of dose resulting from absorption of high energy roentgen rays in this manner has been developed by Cassen, Corrigan and Hayden,[2] and also applied to the betatron by Johns *et al.*[5] Our measurements indicate that in the relation

$$D_d \sim \left(\frac{S+4}{S+d}\right)^2 (e^{-\mu d} - e^{-\mu_s d})$$

the value of μ is 0.023 cm.$^{-1}$ and that of $\mu_s = 0.75$ cm.$^{-1}$ based on the large diameter field data to minimize scatter loss.

Operation of the cylindrical ion chamber by remote control in the water phantom has made it convenient to adjust the number and size of disks in the filter to obtain isodose surfaces of a desired shape. The configuration of the ensemble of disks was determined by calculation and then altered empirically as required by ion chamber measurements. Steep dosage gradients and discontinuities exist along the geometrical edge of the beam. Densitometry of films with a 2 mm. light spot gave detailed information of isodose configurations in this region. Isodose surfaces obtained with 2.5 cm., 5.0 cm., 10.0 cm., and 15.0 cm. diameter fields at 80 cm. skin-target distance with alumidum filters are presented

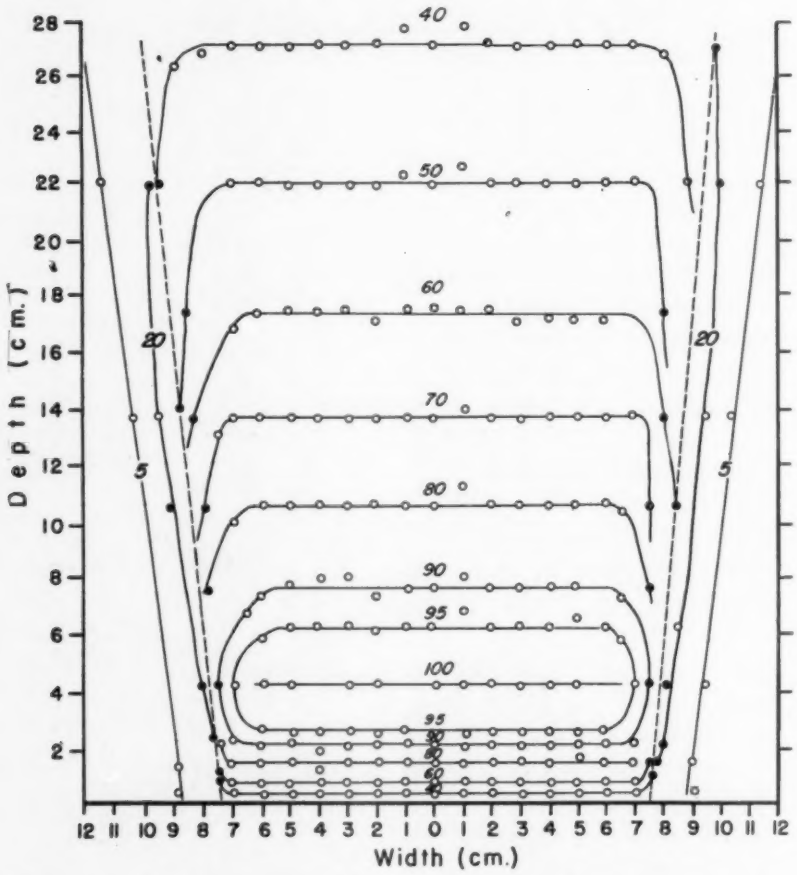

FIG. 15. Isodose distribution for 15.0 cm. diameter field at 80 cm. skin-target distance. Open circles represent ionization chamber data and solid circles represent film data.

in Figures 12, 13, 14, and 15 respectively. Open circles represent ion chamber data, while solid circles represent data obtained from film densitometry. Additional rectangular fields and circular fields of intermediate diameters are also available. In actual practice, in order to minimize exit dose, no skin-target distance greater than 80 cm. has been used or is contemplated. All of the distributions shown are for cases where the surface was normal to the beam direction. For cases of oblique incidence, an approximate relation has been established relating the acute angle ϕ between the skin surface and beam direction and the acute angle θ formed by the actual plane of the isodose surfaces and the beam direction. This relation is $\theta = (90\phi)^{1/2}$.

The techniques employed in these measurements are also being used to measure dose distributions obtained with the direct electron beam which has been successfully extracted from our betatron. These measurements precede the actual use of electrons in experiments planned with animals and eventual human therapy.

SUMMARY

The conversion of a conventional betatron for medical therapy is described. The roentgen-ray beam has been collimated so as to minimize neutron production and has been shielded effectively in such a manner as to permit accurate and rapid alteration of field size. The output of the betatron is monitored with an ion chamber and is integrated to control the exposure.

Techniques for accurate and reproducible dosage measurement with both films and with small ion chambers used with D. C. amplifiers have been developed. Depth dose measurements establish a definite though limited dependence of depth dose on field size. Isodose surfaces have been conveniently controlled with a differential filter and typical distributions are presented which also indicate discontinuities along the geometrical edge of the beam.

The authors wish to express their particular appreciation to Mr. F. Spongberg for his ingenuity in the fabrication of apparatus, and to Mr. W. D. Davies for assistance in operation.

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DEPARTMENT OF TECHNIQUE

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A PRACTICAL COMPRESSION DEVICE FOR SPOT ROENTGENOGRAMS*

By WALLACE S. TIRMAN, M.D., *and* ALLAN C. NICKEL, M.D.
BLUFFTON, INDIANA

MANY devices have been described for use on spot film equipment for compression films in gastrointestinal roentgenography. Generally speaking, these instruments possess one major objection. They usually consist of a rigid cone attached to a metallic base. The lack of a soft pliable compression cone makes it difficult to obtain satisfactory films of the regions near bony prominences, such as the upper portion of the stomach or occasionally the cecum. In addition, with the exception of one recent publication,[1] these devices do not allow for a variable depth of compression.

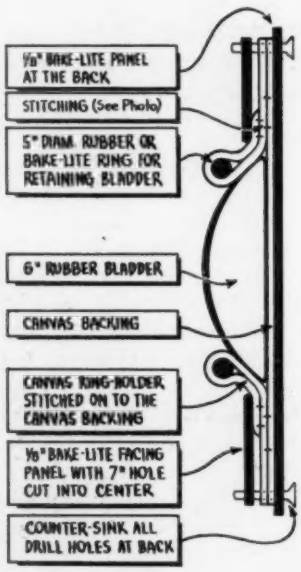
1/8" BAKE-LITE PANEL AT THE BACK
STITCHING (See Photo)
5" DIAM. RUBBER OR BAKE-LITE RING FOR RETAINING BLADDER
6" RUBBER BLADDER
CANVAS BACKING
CANVAS RING-BOLDER STITCHED ON TO THE CANVAS BACKING
1/8" BAKE-LITE FACING PANEL WITH 7" HOLE CUT INTO CENTER
COUNTER-SINK ALL DRILL HOLES AT BACK

FIG. 1

Figures 1, 2 and 3 demonstrate a compression device which overcomes these two objections and presents some further advantages. The device is constructed of bakelite and canvas and a rubber balloon. It is made so that it can be placed on most spot film equipment by sliding it in the grooves on the patient's side of the spot film device. The rubber balloon is the part used for compression and is held in place by canvas and a semisolid rubber ring. The back plate (*E*, Fig. 3) is cut from 1/8 inch bakelite. The dimensions shown may have to be varied to fit the stops and channels of different types of spot film devices. On the patient's side of this plate is pasted the canvas back (*C*, Fig. 3) on which is sewed the canvas ring holder (*B*). The rubber ring present within this is semisolid. The balloon fits between the canvas and the ring holder. The rubber tubing can be attached to the roentgenologist's side of the spot film device. The face plate (*A*, Fig. 3) is cut from bakelite and is slightly smaller at the top and bottom to allow the back plate to fit in the grooves, usually present on spot film devices. The device is then riveted or bolted together.

When assembled and put in place, the roentgenologist can vary the size of the area of compression by inflating or deflating the balloon. The degree of compression varies from nothing to about $3\frac{1}{4}$ inches.

The compression portion is not rigid and therefore cannot impinge on the costal margin and allows for more satisfactory

* From the Caylor-Nickel Clinic, Bluffton, Indiana.

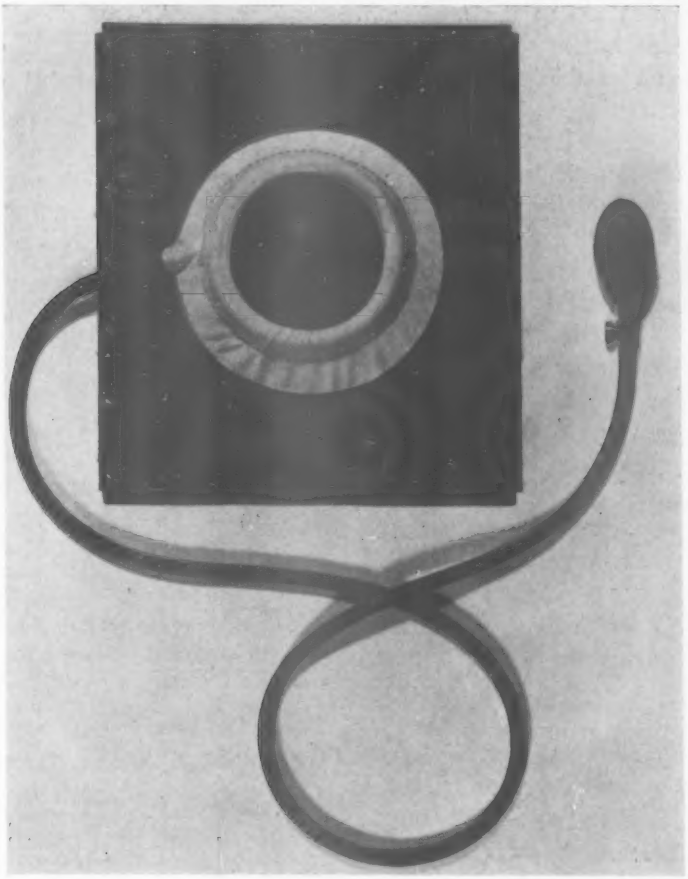

Fig. 2

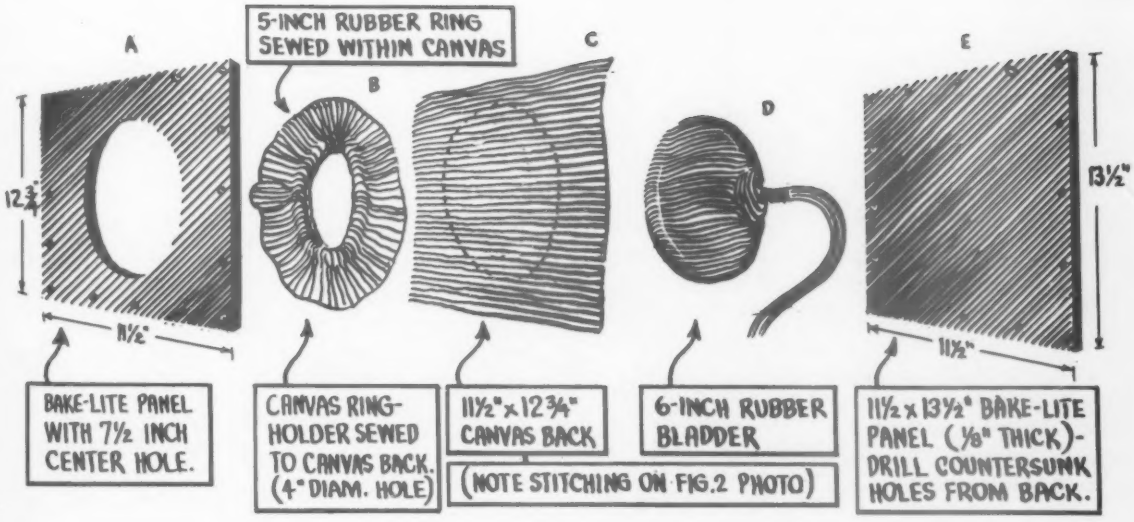
A
5-INCH RUBBER RING SEWED WITHIN CANVAS
B
C
D
E
12¾"
11½"
13½"
11½"
BAKE-LITE PANEL WITH 7½ INCH CENTER HOLE.
CANVAS RING-HOLDER SEWED TO CANVAS BACK. (4" DIAM. HOLE)
11½" x 12¾" CANVAS BACK
6-INCH RUBBER BLADDER
11½ x 13½" BAKE-LITE PANEL (⅛" THICK)- DRILL COUNTERSUNK HOLES FROM BACK.
(NOTE STITCHING ON FIG. 2 PHOTO)

Fig. 3

films of the upper portion of the stomach. Since it contains no radiopaque material, the entire device can be left in place all of the time during roentgenoscopy and the balloon can be inflated when it is needed. This makes the obtaining of compression films considerably less time consuming.

Another important feature is that pressure with the balloon can be substituted for palpation of the stomach with the hand. The portions of the stomach which are accessible to the hand, as a rule, can be compressed with the balloon. This makes it rarely necessary for the roentgenologist to put his hand in the field of radiation. Although at times it may be necessary to palpate the stomach, the rubber balloon, when inflated to the size of about $2\frac{1}{2}$ inches, serves this purpose very satisfactorily. The device also presents one other quality which is desirable. When a compression study is made, the entire film is exposed. The portion of the stomach which is not compressed is demonstrated on the film. This permits observation of portions of the stomach which are adjacent to the area of compression and which would ordinarily be excluded on the usual type of compression film.

CONCLUSIONS

A rubber compression device for spot roentgenograms of the gastrointestinal tract has been described. This can easily be adapted to any type of spot film device. It presents the following characteristics:

1. Its construction is simple and economical.
2. It is not rigid and therefore can compress areas which would be inaccessible with a rigid cone.
3. The depth of palpation can be controlled.
4. It can always be left in place so that no time is lost when compression films are desired.
5. Since the device contains no radiopaque material, the entire film is exposed.

We are indebted to Mr. Harry Lindstrand for preparing the illustrations and to Mr. Harry Hurst for technical assistance.

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EDITORIALS

THE TWO HUNDREDTH ANNIVERSARY OF THE FOUNDING OF THE PENNSYLVANIA HOSPITAL

ON THE eleventh of this month (May, 1951) the Pennsylvania Hospital, Philadelphia, Pennsylvania, will observe the beginning of its third century as the Nation's first hospital. It was founded in 1751, largely through the efforts of Benjamin Franklin and of Dr. Thomas Bond, who was one of early America's leading physicians. "Although in his 'Autobiography' Franklin distinctly disclaims the credit of first suggesting the project, ascribing it to Dr. Thomas Bond, nevertheless, its successful carrying out was undoubtedly due chiefly to Franklin's influence and efforts."[1] Since its founding the Pennsylvania Hospital has been one of the leading institutions in the country, and the hospital is today a modern institution still serving the public in the highest of medical traditions as it has since its inception. It is estimated that more than 2,200,000 persons, approximately the size of Philadelphia's present population, have been treated at the hospital. Two out of three of those patients have been treated free, or were charged only part of the cost of the treatment.[2]

The Pennsylvania Hospital operates under the Board of Managers system, which system, incidentally, had its beginning at this institution. At the founding of the hospital the members of the Board of Managers were community leaders from various walks of life. That system of management has continued to the present time and members of the board are among Philadelphia's most respected citizens. It is readily understandable that under such boards of management the hospital has continued not only to maintain its high professional standard throughout the years but to be responsible for outstanding accomplishments in various fields of research.

At the Pennsylvania Hospital medical apprentices were trained even before the founding of the Nation's first medical school in 1765. This medical apprenticeship formed the pattern for the system of intern and resident training as we know it today. Here at this hospital was built the first medical amphitheater and here also was founded the first public dispensary in the United States. With the opening of the Pennsylvania Hospital a new era in the care and cure of the mentally afflicted began. Prior to the founding of this institution such patients had been regarded as outcasts from society, destined only for confinement in chains and behind bars.

It has been stated, and rightfully so, that the list of some of the physicians who first served the hospital reads like a medical "Who's Who" and includes, in addition to Dr. Thomas Bond, such notables as Dr. Philip Syng Physick, "the father of American surgery"; Dr. William Shippen, Jr., who was the first to establish systematic medical training in America; Dr. Caspar Wistar, famous anatomist, and credited with the first medical textbook in this country; Dr. John Morgan, founder of the University of Pennsylvania School of Medicine; Dr. Benjamin Rush, "the father of psychological medicine"; and Dr. Thomas Story Kirkbride, pioneer in the care of the mentally ill. With such eminent

[1] Packard, Francis R. Some Account of the Pennsylvania Hospital, From its first Rise to the Beginning of the Year 1938. Engle Press, Philadelphia, 1938.

[2] The 200th anniversary of the first hospital in the United States of America—the Pennsylvania Hospital, Philadelphia, Pennsylvania. *Bull. Am. Coll. Surgeons*, January, 1951, *36*, 64–65.

physicians staffing the institution in its beginnings, it is small wonder that it has been able to maintain the high standards of its professional staff throughout these two hundred years.

Unlike many institutions, the Pennsylvania Hospital has cherished through the years various symbols of its traditions and has preserved them. As an example, in the newel posts of "the great staircase" of the center building there can still be seen wooden amity buttons placed there by the original contractor to indicate for posterity that harmonious relations existed between employer and employed during the construction of the building.

At their meeting on July 6, 1751, the Board of Managers chose Joshua Crosby as their president and Benjamin Franklin as clerk and one of the most valued treasures in the possession of the hospital today is the first minute book of the proceedings of the board which is partly in the handwriting of its first clerk (Benjamin Franklin). Interestingly enough, one of the rules adopted by the committee appointed by the managers for that purpose was that any manager who was late for a meeting should be fined one shilling and if absent two shillings. Franklin decided that the correct time for purposes of fining should be determined according to the town clock and if the clock failed, the watch of the eldest person present should determine the fine. The present Board of Managers still observes the custom begun in Franklin's time and still imposes fines on members who are tardy or absent.

It is of scientific interest, and perhaps a point somewhat neglected in these days, that in the early days of the hospital great importance was placed on the effect of weather and seasons upon diseases. Because of this, Dr. Bond gave the hospital a meteorological device for the recording of weather conditions. Thus the Pennsylvania Hospital kept the first systematic weather records ever maintained in this country, and it is reported that these records were often used in early court proceedings when litigation concerning the weather arose.

In its first few months of existence, the Pennsylvania Hospital had only three regularly attending physicians, four consultants, a matron to care for the house, and twenty-three patients. As the years passed and the hospital grew, it is quite understandable that the size of the staff and non-professional personnel increased; so today, in two major departments, namely the Department for the Sick and Injured and the Department for Mental and Nervous Diseases, there are 21,000 annual admissions, and their out-patient clinics record from 150,000 to 200,000 visits by ambulant patients each year. Personnel, including medical, administrative, and other employees, numbers more than fifteen hundred.

Of the more than 150,000 patient visits in the Out-Patient Department, over 65 per cent are free of charge. Apart from this, the Out-Patient Department provides medical students with valuable training. It is of interest to note that of the approximately 210 m mbers of the present visiting medical staff, more than 66 per cent have been certified as specialists. The hospital's charitable work is made possible primarily through the generosity of contributors and its extent is limited only by the amount of contributions that are received. While Community Chest donations and state aid have helped, most of the needs of the hospital have been met by private individuals.

It is of historical interest to note that the Pennsylvania Hospital, during its two hundred years of existence, has cared for soldiers from the Revolutionary War, the War of 1812, the Civil War, the Spanish-American War, World War I and World War II. In 1916, the late Dr. Richard H. Harte, one of the surgeons to the Pennsylvania Hospital, with the cooperation of the Board of Managers organized a Base Hospital Unit in World War I, which was known as Base Hospital No. 10.

Shortly after Röntgen's announcement

of the discovery of the x-ray in 1895, an x-ray apparatus was installed at the Pennsylvania Hospital (1897). For a number of years, as in most hospitals at that time, its use was limited to making roentgenograms for diagnostic purposes of suspected fractures or to locate foreign bodies in the digestive and respiratory tracts. The duty of taking the x-ray plates was assigned to the Chief Resident. As the importance of the science of roentgenology grew, it became necessary to place the work in charge of a skilled roentgenologist and in 1912 Dr. David R. Bowen was appointed to head the new department, the first to hold such a position in the hospital. Dr. Bowen remained in charge of the Department of Roentgenology until his resignation in 1931.

When the Board of Managers of the Pennsylvania Hospital selected Dr. Bowen as their first roentgenologist they were following the pattern which had influenced other Boards of Managers of the hospital in selecting the best obtainable. Dr. Bowen made many contributions to roentgenology, particularly in its technical aspects. While head of the department he developed a splendid and efficient organization and, since he was meticulous in his technique, his roentgenological procedures were based on exacting methods and this, coupled with honest efforts of interpretation, stamped him as a man of rare ability. His interest in the technical aspects of roentgenology was the occasion for his appointment as Editor of the Department of Technique of this JOURNAL, a position which he held for a number of years.

Upon the resignation of Dr. Bowen in 1931, Dr. Paul A. Bishop who had held the position of Assistant Roentgenologist since 1925 was chosen to head the Department of Roentgenology. In the twenty-five years that Dr. Bishop has been associated with the Department as Assistant and Chief he has seen and participated actively in marked advances and developments in the application of radiology not only in its diagnostic and therapeutic aspects in the daily care and treatment of patients but also in its use in the broader fields of experimental research. A recent honor which has come to Dr. Bishop and which is indicative of his outstanding abilities as radiologist, physician and administrator is his recent election as President of the Staff of the hospital. His hosts of friends in the medical world join him and the other members of the staff of the Pennsylvania Hospital in the celebration of the Two Hundredth Anniversary of its founding.

As far back as 1773 Benjamin Franklin expressed a wish. "Having a very ardent desire to see and observe the state of America a hundred years hence," he wrote, "I should prefer to any ordinary death, the being immersed in a cask of Madeira wine, with a few friends, till that time to be recalled to life by the solar warmth of my dear country."[3] If Benjamin Franklin could be recalled to life by the solar warmth of his own dear Philadelphia in the month of May, 1951, it is certain that nothing he would behold in all of his varied efforts would give him more pleasure than to see the high place which the Pennsylvania Hospital occupies in the medical world, a hospital which he was instrumental in founding in the good year 1751.

[3] *New York Times*, Jan. 16, 1951, p. 31.

LAWTHER JACKSON WHITEHEAD
1891-1951

ON THE morning of February 26, 1951, Dr. Lawther Jackson Whitehead died at the age of fifty-nine years, following an illness of approximately three months. He was born at Scotland Neck, North Carolina, the son of Andrew Jackson and Lucy Doles Whitehead.

At the age of eighteen years, he entered Davidson College where he spent three years preparatory to the study of medicine which he began at the Medical College of Virginia in 1912. Over a span of forty years, this latter institution successively honored him with the degree of "doctor of

medicine" (1916), and the appointments of assistant in roentgenology (1922), instructor (1924), associate (1927), assistant professor of radiology (1936), associate professor (1941), and professor of clinical radiology (1950).

It is known that, during the last fifteen years in the various professorial ranks, he was never late to, or missed, a scheduled lecture at the medical college and that he was the radiologic consultant most frequently called upon for advice and actual film interpretation by the younger men. His early academic promotions by the late Dr. Alfred L. Gray prove the esteem that pioneer held for him, for his work at the college.

The Johnston-Willis Hospital, concurrently claimed Dr. Whitehead's attention for thirty-five years, from 1916 to 1951, with the exception of the World War I years which were devoted to the formal study of roentgenology in the rigid Army Courses of that period which included a station at that ever famous radiologic city—Rochester, New York. This training was preceded by a most valuable two year internship at the hospital under the leading surgeons of Richmond of that day. Following the war, he became associated with Dr. Daniel D. Talley, Jr., at both the hospital and in the private practice of roentgenology.

In 1936, Dr. Whitehead was admitted into active membership in the American Roentgen Ray Society. He had previously been made a member of the Richmond Academy of Medicine, Medical Society of Virginia, American Medical Association, American College of Radiology and the Southern Medical Society. Of the latter, he was vice-president, Section of Roentgenology, 1944, and president of the section, 1945. He was a diplomate of the American Board of Radiology.

Dr. Whitehead's research was in the field of uterotubography in which he was closely associated with Dr. M. Pierce Rucker. Four of their joint papers, pioneer work in the field, appeared in state, obstetrical and radiological journals, including the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, some twenty-three years ago. A more recent textbook on clinical radiology had the bulk of its gynecologic illustrations supplied by Dr. Whitehead.

As a consultant in medicolegal problems, Dr. Whitehead had no near rivals. His advice to attorneys for Lloyd's of London and leading American insurance companies was in constant demand and is definitely known to have kept many lawsuits out of the courts.

During World War I, he had one year of service in France with Base Hospital 19, serving as a First Lieutenant and later as Captain in the Army Medical Corps. An additional year was spent in this country.

On October 25, 1927, Dr. Whitehead married Eleanor E. Enslow. One daughter, Mrs. Robert P. Buford, Jr., of Richmond, a grandson Robert P. Buford, III, also two sisters, Mrs. P. E. Lucas, of Burgaw, N. C., and Mrs. L. B. McDaniel of Tarboro, N. C., and three brothers, Julius Whitehead and Turner Whitehead of Scotland Neck, and Dr. Seba Whitehead, of Asheville, N. C., survive him.

He attended St. Paul's Episcopal Church, Richmond, where funeral services were held, with burial in Hollywood Cemetery.

He was a member of the Country Club of Virginia where his useful work paralleled that of his medicolegal activities in that it was almost wholly "behind the scenes" and distinctly not in the "spotlight." At the Richmond Academy of Medicine as at American Roentgen Ray Society meetings, he sat on the right well towards the front listening attentively. Ten years ago, at the Cincinnati meeting of the American Roentgen Ray Society, he listened to every one of the fifty papers during the four day session.

Dr. Whitehead set standards of hard work and humility we should strive to equal.

FREDERICK B. MANDEVILLE, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 25–28, 1951.

American Radium Society
Secretary, Dr. J. E. Wirth, U. S. Marine Hospital, Baltimore, Md. Annual meeting: Hotel Claridge, Atlantic City, N. J., June 7–9, 1951.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Annual meeting: Palmer House, Chicago, Ill., Dec. 2–7, 1951.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6.

Section on Radiology, American Medical Association
Secretary, Dr. P. C. Hodges, 950 E. 59th St., Chicago, Ill. Meets Atlantic City, N. J., June 11–15, 1951.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

Arizona Association of Pathologists and Radiologists
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. J. D. King, 35 Linden Ave., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. B. D. Braun, 6 N. Michigan Ave., Chicago 2, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cincinnati Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. R. Hannan, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Paul E. RePass, 306 Republic Bldg., Denver 2, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. J. C. Cook, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. T. H. Lipscomb, 30 W. Beaver St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Cincinnati Radiological Society
Secretary, Dr. Lawrence Gibboney, Carew Tower, Cincinnati 2, Ohio. Meets first Monday of each month.

Greater Miami Radiological Society
Secretary, Dr. T. M. Berman, 350 Lincoln Rd., Miami Beach, Florida. Meets last Wednesday of each month at 8:00 P.M. at Veterans Administration Regional Office.

Houston Radiological Society
Secretary, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. C. F. Miller, Central Maine General Hospital, Lewiston, Maine.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, Sept. to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. R. W. Blanchard, 1216 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. L. L. Robbins, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. L. Olpp, 49 Ivy Lane, Tenafly, N. J. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. W. Wauters, 701 High St., Auburn, Calif. Meets at dinner last Monday, every second month, except June, July and August.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio. Meets Ft. Hayes Hotel, Columbus, Ohio, May 25–27, 1951.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, 21st & Xanthus, Tulsa 4, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. C. T. Jessell, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual meeting, May 18 and 19, 1951, at William Penn Hotel, Pittsburgh, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. G. P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, Sept. to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. K. C. Corley, 1835 Eye St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, Jan., March, May, Oct. at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Peter Gianquinto, 685 High St., Newark, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. George Gamsu, 191 S. Goodman St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets August 9, 10, 11, 1951, at Denver, Colorado.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. D. S. Bottom, 510 S. Kingshighway, St. Louis, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Tuesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. S. H. Fisher, 107 E. North St., Greenville, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Meets Houston, Texas, Jan. 18 and 19, 1952.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. R. C. Kiltz, 705 Medical-Dental Bldg., Everett, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

Wisconsin Radiological Society
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. M. A. Sisson, 450 Sutter St., San Francisco, 8, Calif. Meets Jan. to July, Lane Hall, Stanford Univ. Hospital; July to Dec. San Francisco Hospital.

Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86 Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. de G. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro, Sede, Cordoba
President, Prof. Dr. David L. Caro, Cerro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Torres Focke, Av. 34, No. 17–34, Bogota, Colombia. Meets last Wednesday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

INDIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India

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OHIO STATE RADIOLOGICAL SOCIETY

The Eleventh Annual Meeting of the Ohio State Radiological Society will be held at the Fort Hayes Hotel, Columbus, Ohio, on Friday, Saturday and Sunday, May 25, 26 and 27, 1951. The following program will be presented:

Friday, May 25

Golf in the afternoon with dinner at the Country Club.

Saturday, May 26

9:00–9:30 A.M. The Urologic Problems in Pediatric Diagnosis. By Dr. Fred Silverman.
9:30–10:00 A.M. Abdominal Aortography. By Dr. Ben Felson and Dr. Arthur Evans.
10:30 A.M. Fluoroscopy in Conjunction with Retrograde Pyelography. By Dr. E. C. Baker and Dr. F. A. Miller.
11:00 A.M. Visualization of the Intervertebral Disc with Diodrast. By Dr. Robert Wise.
2:00 P.M. Carcinoma of the Cervix as Studied at the Cincinnati General Hospital for the Past Eleven Years—Complications, Treatment, and Results. By Dr. Charles Barrett.
2:45 P.M. Contact Therapy and Its Treatment of Superficial Lesions. By Dr. Robert Hayes.
7:30 P.M. Dinner, Entertainment, Dancing.

Sunday, May 27

10:00 A.M. to 12 noon. "Stump the Experts"—Diagnosis. Moderator, Dr. Clarence Hufford. Panel—Dr. Ben Felson, Dr. John R. Hannan, Dr. Joseph L. Morton, Dr. James G. Tye.
2:00–4:00 P.M. "Information Please"—Therapy. Moderator, Dr. Robert Hayes. Panel—Dr. Charles Barrett, Dr. Harry Hauser, Dr. Edward T. Kirkendall, Dr. W. S. Peck.

AMERICAN SOCIETY OF X-RAY TECHNICIANS

The Twenty-third Annual Convention of the American Society of X-Ray Technicians will be held from June 3 to 8, 1951, at the Benjamin Franklin Hotel, Philadelphia, Pennsylvania. The President is John Cahoon, R. T., Duke University Hospital, Durham, North Carolina, and the Convention Chairman is Harry Y. Ball, R. T., Bryn Mawr Hospital, Bryn Mawr, Pennsylvania.

COURSES IN RADIOISOTOPE TECHNIQUES AND RADIOAUTOGRAPHY

Three additional basic courses in radioisotope techniques of four weeks' duration and a three week radioautography course will be offered this summer by the Special Training Division of the Oak Ridge Institute of Nuclear Studies.

The basic courses will be the 21st, 22nd, and 23rd to be given by the Institute since the program was initiated in June, 1948. They are scheduled to begin on June 11, July 9 and August 15, 1951. The courses combine lectures, demonstrations, and laboratory work. Sufficient space is available to permit individual laboratory work. Thirty-two participants will be accepted for each course.

The radioautography course which will begin on July 2 will be the first of its kind to be offered by the Institute. It is intended for personnel who will direct medical or biological research utilizing the radioautographic process.

George A. Boyd, formerly of the Uni-

versity of Rochester, who is well known for his work in radioautography, will direct the course. Subjects to be covered include the theory of the photographic process, reaction of ionizing particles with photographic emulsions and the interpretation of results, and techniques of making gross and microscopic radio autograms. Twenty participants will be accepted for the course.

Registration is $25 for each course. Additional information and application forms are available from Ralph T. Overman, Chairman, Special Training Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

ATLANTA RADIOLOGICAL SOCIETY

At the March meeting of the Atlanta Radiological Society, the following officers were elected for the coming year: *President*, Dr. Albert Rayle, Sr.; *Vice-President*, Dr. Leonard Long; *Secretary-Treasurer*, Dr. J. Dudley King.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, NEW YORK

At the annual meeting of the Rochester Roentgen Ray Society held in December, 1950, the following officers were elected for 1950–1951: *President*, Dr. Ralph E. Alexander; *Vice-President*, Dr. A. Vaughn Winchell; *Secretary-Treasurer*, Dr. George Gamsu, all of Rochester, New York. Meetings will be held on the last Monday of each month, from September through May, at Strong Memorial Hospital.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

RADIOGRAPHIC ATLAS OF SKELETAL DEVELOPMENT OF THE HAND AND WRIST. Based on the Brush Foundation Study of Human Growth and Development initiated by T. Wingate Todd, M.B., Ch.B., F.R.C.S., Late Henry Willson Payne Professor of Anatomy in Western Reserve University School of Medicine. By William Walter Greulich, M.A., Ph.D., Professor of Anatomy, Stanford University School of Medicine, etc.; and S. Idell Pyle, M.S. Research Associate, Brush Foundation and Department of Anatomy, Western Reserve University School of Medicine. Cloth. Price, $10.00. Pp. 190, with numerous illustrations. Stanford University Press, Stanford, California, 1950.

We have known established and reputable radiologists who were impatient or had a mildly tolerant attitude concerning pediatricians who insisted on accurate and specific information regarding growth and development from roentgenographic views of the hand and wrist. Such a study was our first method for gross determination of disturbances of metabolism. However, the information obtained seemed inadequate for precision work and variations within apparently normal individuals was found to be so great that there has been a tendency to discourage the use of the hand and wrist as a gauge of general body growth. For a long time we have employed additional films of various other parts of the body to aid in our diagnosis but with results not greatly improved.

This new book on the hand and wrist may well change the roentgenologist's ideas on the subject. Careful reading of the preface, study of the rationale and technique used in developing standards, and following the detailed instructions for proper assessment of the appearance of the bones of the hand and wrist is very enlightening. It seems quite probable that in the case of the authors, a single roentgenogram of the hand can give more information as to growth and development than films of the entire skeleton give to the average roentgenologist. They believe that sexual and general physical maturation are closely related to the development of the hand and wrist and that much additional information as to bone structure, such as mineral salt content and arrest of development due to illness can also be obtained from the study of a hand and wrist film.

Dr. Greulich is Professor and Head of the Department of Anatomy at Stanford University School of Medicine. Miss Pyle is Research Associate, Brush Foundation and Department of Anatomy of Western Reserve University School of Medicine. They give due credit to the genius and industry of Dr. T. Wingate Todd, who inspired this work and who published the "Atlas of Skeletal Maturation of the Hand" in 1937, using part of the material from this Research Series. They, however, point out that this book provides a more complete and uniform standard than did Dr. Todd's "Atlas." They admit its limitations when applied to various races or nationalities where standards of living and hygiene affect growth and development but they believe it furnishes standards from which comparisons can readily be made.

Thirty-five pages of text are followed by the same number of full page negative reproductions of male standards with a page of descriptive material opposite. A similar group of female standards is given and there follows a fourth section devoted to maturity indicators of individual bones and epiphyses with numerous line drawings explaining the appearances found in each standard.

By use of this book, periods of growth between appearance of ossification centers and full development with final closure of epiphyseal lines may be studied eliminating periods in which it has been considered that roentgenograms of the hand and wrist were of little value. We recommend it to all radiologists, pediatricians, and endocrinologists who are trying to do good work and wish to improve their diagnoses.

E. W. HALL, M.D.

Lehrbuch der röntgenologischen Differentialdiagnostik. Band I. Erkrankungen der Brustorgane. Von Werner Teschendorf, Köln. Zweite Auflage. Cloth. Price, DM 84.–. Pp. 779, with 865 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1950.

Lehrbuch der röntgenologischen Differentialdiagnostik. Band II. Erkrankungen der Bauchorgane. Von Werner Teschendorf, Köln. Zweite Auflage. Cloth. Price, DM 72.–. Pp. 608, with 1,081 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1950.

A large number of excellent radiologic texts of the pre-World War II years is coming out of Germany in enlarged and revised editions. They are conspicuous for the excellence of the illustrations and the high grade of press-work on good paper. The present work is an example of such recent publications. Many American radiologists have long been familiar with the first edition of this well arranged and illustrated work on roentgen diagnosis in internal medicine. The arrangement and general appearance of the revised edition is much like the pre-war publication of 1939 but much enlarged. The type is smaller and more compact but easily read; the text is somewhat increased. A few additional illustrations are included. In his efforts to make the work one for easy reference, the author has adopted a very useful system of classification of diseases, greatly facilitating its usefulness. Stress is laid upon the differential diagnosis, as the title indicates. Numerous references to world literature are cited, some of them fairly recent. Many more publications from the United States might well have been included in the references. Several months of study and utilization of this work in daily practice convinces your reveiwer that it is a highly useful and valuable addition to the radiologist's library, and of great importance as a reference for internists.

James T. Case, M.D.

Le zone polmonari. By Lucio di Guglielmo. Cardboard. Price, L. 2,800. Pp. 303, with 231 illustrations. Edizioni Scientifiche Italiane, Galleria Umberto I, 83, Napoli, Italy, 1950.

The old anatomical division of the lungs into the various lobes has been recently refined by subdividing the lobes into pulmonary segments. This conception stems from the fact that although the segments are not separated by pleural fissures, they are supplied by independent bronchovascular branches and are actually separated from the adjacent segments by loose connective tissue. This separation of the lobes into segments was comparatively unimportant until a few years ago, but the great progress by the thoracic surgeons has made the subdivision of great practical interest. Many surgeons today prefer to excise only the effected segment, thus saving part of the vascular and alveolar territory of the whole lobe.

Another application of the segmental division of the pulmonary lobes is the precise administration of various medications (penicillin, streptomycin). With this in mind, Dr. Guglielmo has collected in his book a great deal of the available information. This book is of great interest to all radiologists who have to localize lung lesions not only as to the lobe, but also as to the segment involved.

The first part of the book is devoted to the history of the subject and to the anatomic structure of the pulmonary segments. The anatomic autonomy of the pulmonary segments is explained in great detail and the technique of bronchographic, bronchoscopic and laminagraphic study of the segments is shown.

The second part of the book describes each segment, its confines and its relationship with other segments of the lungs. The third part of the book shows how a knowledge of segmental anatomy is useful in interpreting pulmonary pathology, whether it involves the parenchyma, the bronchi or the vascular elements. A detailed description of the diagnostic and therapeutic applications follows, especially regarding localized bronchography, localized application of penicillin and segmental surgical procedures. The book is well organized, well written and well illustrated and the author should be congratulated for bringing to the attention of radiologists a subject which will become more and more important in the future.

Cesare Gianturco, M.D.

The Results of Radium and X-Ray Therapy in Malignant Disease. Being the Third Statistical Report from the Radium Institute, The Christie Hospital and Holt Radium Institute, Manchester. Years 1940 to 1944 inclusive assessed at 5 years and 1934 to

1938 assessed at 10 years. Compiled by Ralston Paterson, Margaret Tod and Marion Russell. Cloth. Price, $2.50. Pp. 167, with numerous tables. E. & S. Livingstone Ltd., 16–17 Tevoit Place, Edinburgh, Scotland, 1950.

This book is the third five year report presented by the Holt Radium Institute. It deals with the cases treated from 1940 to 1944, the period of World War II. In spite of the fact that during this period new building was impossible and new apparatus could only be obtained with the greatest difficulty, and the staff was reduced by claims of the services, the number of cases treated between 1940 and 1944 was 15,226. The wards were always full. It was a period when it was almost impossible to replace trained radiotherapists who went into the service and yet it was during that time that the training period was continued uninterruptedly. Another difficulty presented by the circumstances was maintaining the high standard of radium therapy.

The increased number of patients cared for during this period was explained somewhat by complete centralization so far as radium was concerned due to the safety regulations which govern its use.

This report continues the policy previously adhered to. Part I begins with a general survey of the effects of treatment on malignant disease. In Part II, there is an analysis of the results of treatment to allow one to see the progress in certain types of treatment. Part III refers to cases which have already been reported and shows position of the treatment at the tenth anniversary.

The statistical method used is of a high order and should be read by everyone interested in reporting the effect of treatment on certain diseases. Some of the principles emphasized in this report are the following:

1. Essential facts are given but without producing an impression of confusion by giving too many facts at one time.

2. All relevant figures are shown.

3. In presenting the percentage results, the authors give net survival percentages and the crude survival percentage. The various figures were based on actuarial methods of life table construction in order that one can get a true estimate of the treatment employed.

This little book serves as a model to any who are concerned with making a critical study of cases being treated. Ordinarily one would not find such a report interesting reading, but this reviewer had the opposite experience in studying this book. The comments made by the authors in discussing each category being analyzed are most stimulating and helpful.

The publishers have assisted the authors in presenting this work in a most attractive way.

E. P. Pendergrass, M.D.

Radiation Therapy in the Management of Cancer of the Uterine Cervix. By Simeon T. Cantril, M.D., Director, Tumor Institute of the Swedish Hospital, Seattle, Washington. Cloth. Price, $5.00. Pp. 196, with 25 illustrations and 29 tables. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

This monograph of two hundred pages includes an appendix on the staging of cancer of the uterine cervix of the League of Nations, 1937, with illustrative diagrams of the various stages. There is also an appendix on dosimetry in intracavitary radium therapy based on the work of the Manchester group.

In his introduction, Dr. Cantril states his intent of reviewing important clinical and pathological features of cancer of the cervix which bear upon its management by radium and roentgen therapy. Dr. Cantril's review of clinical complications, symptoms and signs of cancer, his description of the growth and spread of cancer of the cervix, all make very interesting reading to the experienced radiologist and should be most valuable to the student. His many illustrations are well chosen to show the relation of the various pelvic organs and vessels and the manner in which cancer spreads by direct invasion and lymphatic metastases. The difficulty in differentiating between inflammatory changes in the parametrium and cancer invasion is particularly well pointed out, and the clinician is warned to be careful of his prognosis based on pelvic examination, even in the early stages.

His chapter on complications of cervical cancer (pelvic infection, hemorrhage, urinary complications, and gastrointestinal complications) is well and carefully written. One finds very little that can be added or adversely criticized in what he has to say.

Although Dr. Cantril uses the classifications of the League of Nations in the staging of

cancer of the cervix, it is easy to see that he is not entirely satisfied that it is of real prognostic value. He notes several discrepancies. With all its faults, however, he still feels that some such classification is necessary and that that offered by the international body is the best yet offered.

The need for careful biopsy is emphasized. Dr. Cantril has written a fine chapter on radiation therapy and has given an excellent historical review of the development of the intracavitary technique based on the work of the Stockholm, Paris and Manchester groups.

He has pointed out that there is more than one way to treat cancer of the cervix and that individuals will vary in their techniques and yet all are essentially agreed on the fundamental principles. Dr. Cantril has well emphasized the importance of the individualization of each patient with the ability to adapt the apparatus at hand to all manifold differences as they present themselves: size of the pelvis, size of the vagina, course of invasion, presence of infection, and all the other multiple factors that one finds. The best results have been attained by the man experienced and interested in his field who has carried out the treatment or closely directed it.

Chapters on transvaginal and external roentgen therapy are given. There is also a paragraph on the combined pelvic dosage. In the use of external and transvaginal roentgen irradiation as adjunctive treatment, Dr. Cantril has gone into some of the dangers of overirradiation that may occur. His paragraph on complications of radiation therapy is well written and includes most of the familiar types of complications with suggestions as to their avoidance. Dr. Cantril has given a chapter on results of treatment with intracavitary radiation alone or with roentgen radiation in combination. He also has a chapter on surgery in the management of cancer of the cervix. Of course, it is a little early yet to come to any definite conclusions as to the value of surgery.

On the whole, this monograph is very well written, and Dr. Cantril has said the essential things, particularly as they apply to intracavitary radiation. It may be that he has been limited by his assignment to a discussion of *intracavitary* treatment of cancer of the cervix, but it is a little disturbing to some of us who have had a great interest in the use of *interstitial* radiation and have used this type of radiation over many years with good results to note that he has found no place in his otherwise comprehensive book to even mention that there is such a thing as interstitial radiation in the treatment of cancer of the cervix uteri.

George W. Waterman, M.D.

Über die neuen Strahlenschutzregeln für die Herstellung und Errichtung medizinischer Röntgeneinrichtungen und -anlagen DIN 6811 and 6812. By Dipl.-Ing. Herbert Graf, Oberingenieur der Siemens-Reiniger-Werke A. G., Erlangen. Paper. Price, $1.25. Pp. 72, with several tables. Stuttgart: George Thieme, 1949. (Grune & Stratton, Inc., Medical Publishers, 381 Fourth Street, New York 16, New York.)

This booklet gives in detail the safety rules in force in Germany at present regarding the construction, installation and operation of roentgenologic equipment for medical purposes. It is the close equivalent of our American "Medical X-Ray Protection up to Two Million Volts," Handbook 41, published by the National Bureau of Standards. It is noteworthy to state that the total daily tolerance dose in diagnostic work is set at 0.25 r in general but for the zone of the generative organs at 0.025 r. For all therapy workers the daily tolerance dose should not exceed 0.025 r.

Ernst A. Pohle, M. D.

Some Applications of Nuclear Physics to Medicine. *British Journal of Radiology*, Supplement No. 2. By W. V. Mayneord, D. Sc., F. Inst. P., Professor of Physics applied to Medicine, University of London, Physicist to the Royal Cancer Hospital. Paper. Price, 35s. Pp. 290, with 152 illustrations. British Institute of Radiology, 32 Welbeck Street, London, W. 1., England, 1950.

This excellent monograph covers the subjects of: (a) Nuclear Physics and Isotope Production, (b) Medical Applications of Selected Radioactive Isotopes, (c) Dosimetry of Artificial Radioisotopes, (d) Physics and Dosimetry of High Voltage Radiations, and (e) Scintillation Counting and Its Medical Applications. The chapter on nuclear physics and isotope production is notable for the conciseness and clarity that a busy clinician would welcome in the presentation of this subject.

By limiting the discussion on the use of

radioisotopes in the study of intermediary metabolism, the author has succeeded in treating adequately the present state of the art of beta-ray and gamma-ray dosimetry, and in discussing with imagination many practical aspects on their choice as external and internal radiotherapeutic agents.

The chapters on high voltage radiation review succinctly the mechanisms of particle acceleration and discuss at length the problems of dosimetry and protection in this energy range. A section on clinical applications of high energy quanta represents a unique contribution to the radiological literature, inasmuch as it provides the radiotherapist with some isodose curves obtainable with crossed beams of 20 mev. roentgen rays.

The section on scintillation counters is in the main a report of the original investigations carried out by the author and his colleagues at the Royal Cancer Hospital; it deals with the possible uses which this type of instrument may have in several problems of radiological physics and radioisotope localization *in vivo*.

The book is generously supplied with appendices and bibliographic material which will prove of undoubted value to a serious student of the subject.

The author, his collaborators and their sponsors, are to be congratulated upon having published a very much needed book for the enlightenment and education of radiologists and radiological physicists.

L. D. Marinelli

Infrared Radiation Therapy Sources and Their Analysis with Scanner. By Leopold Rovner, Consulting Physicist, Cambridge, Massachusetts. Fabrikoid. Price, $1.50. Pp. 34, with 21 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

The present book is published as Publication Number 65 of the American Lecture Series as part of the series of American Lectures in Medical Physics.

The heat lamp has been all too commonly used as a source of infrared heat without an adequate knowledge of what it can do, and what its defects and advantages are. The present small book is based on measurements with a special scanning instrument developed at the Medical School of the University of Iowa which is a recording infrared intensity meter. With this meter the radiation patterns of different infrared generators have been examined.

This little book contains valuable material for those who use infrared lamps regularly and want to know exactly what such a lamp can do.

H. D. Bouman, M.D.

BOOKS RECEIVED

Les Isotopes Radioactifs en Médecine et en Biologie. Par Maurice Tubiana, Chef de Clinique à la Faculté de Médecine de Paris; Chargé de Recherches à l'Institut National d'Hygiène. Préface du Pr L. Bugnard. Paper. Price, 1800 fr. Pp. 392, with 84 illustrations. Masson et Cie., 120, boulevard Saint-Germain, Paris 6e, France, 1950.

Vernal Conjunctivitis. By M. N. Beigelman, M.D., Clinical Professor of Surgery (Ophthalmology), University of Southern California School of Medicine; Senior Attending Ophthalmologist, Cedars of Lebanon Hospital; Attending Eye Pathologist, Los Angeles County Hospital. With a Foreword by Sir W. Stewart Duke-Elder, K.C.V.O., M.A., D.Sc. (St. And.), Ph.D. (Lond.), M.D., Ch.B., F.R.C.S., Hon.D.Sc. (Northwestern). Cloth. Price, $6.00. Pp. 430, with 49 illustrations. University of Southern California Press, Los Angeles, California, 1950.

The Preparation of Photographic Prints for Medical Publication. By Stanley J. McComb, F.B.P.A., Section on Photography, Mayo Clinic, Rochester, Minnesota. Fabrikoid. Price, $2.00. Pp. 69, with 21 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

A Symposium on Steroid Hormones. Edited by Edgar S. Gordon. Cloth. Price, $6.50. Pp. 396, with numerous illustrations and tables. University of Wisconsin Press, 811 State Street, Madison, Wisconsin. 1950.

Atti del XVI Congresso Nazionale di Radiologia Medica. Taormina 15–18 Maggio 1950. A cura del Prof. Ettore Castronovo, Messina. Volume I. Relazioni Ufficiali. Parte I. La radiodiagnostica dei tumori cerebrali. By Prof. Fermo Mascherpa. Paper. Pp. 125, with 124 illustrations. Tipografia Ditta d'Amico, Messina, Italy, 1950.

Atti del XVI Congresso Nazionale di Radiologia Medica. Taormina 15–18 Maggio 1950. A cura del Prof. Ettore Castronovo, Messina. Volume I. Relazioni Ufficiali. Parte II. La radioterapia dei tumori maligni del sistema reticoloendoteliale. By Prof. Giovanni F. Gardini. Paper. Pp. 78, with several illustrations and tables. Tipografia Ditta d'Amico, Messina, Italy, 1950.

Atti del XVI Congresso Nazionale di Radiologia Medica. Taormina 15–18 Maggio 1950. A cura del Prof. Ettore Castronovo, Messina. Volume I. Relazioni Ufficiali. Parte III. Radioterapia e radiobiologia dei tumori delle ossa. By Prof. Adamo Grilli, Aiuto Ordinario 1st. di Radiologia Med. Università di Roma, Direttore: Prof. E. Milani. Paper. Pp. 201, with 57 illustrations and numerous tables. Abruzzini Editore, Roma, Italy, 1950.

Selected Papers from the Royal Cancer Hospital and the Chester Beatty Research Institute. Volume V. Paper. Price, 16s. Pp. 483, with numerous illustrations. Published by order of the Board of Governors of the Royal Cancer Hospital, Fulham Road, London, S.W. 3, England, 1945–1947.

Annual Review of Medicine. By Windsor C. Cutting, Editor, Stanford University School of Medicine, and Henry W. Newman, Associate Editor, Stanford University School of Medicine. Volume 1. Cloth. Price, $6.00. Pp. 484. Annual Reviews, Inc., Stanford, California, 1950.

Photons and Electrons. By K. H. Spring, M.Sc. Cloth. Price, $1.75. Pp. 108, with 38 diagrams. John Wiley & Sons, Inc., 440 Fourth Avenue, New York 16, New York, 1950.

Progress in Biophysics and Biophysical Chemistry. Volume I. Editors: J. A. V. Butler, Chester Beatty Research Institute, Royal Cancer Hospital, London; and J. T. Randall, F.R.S., Wheatstone Professor of Physics in the University of London at King's College. Cloth. Price, $6.80. Pp. 279, with numerous illustrations. Academic Press, Inc., Publishers, 125 East 23rd Street, New York, New York, 1950.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Garde, A., and Lévy, A. Bases anatomo-radiologiques. (Les hydrocéphalies de l'adulte.) (The anatomo-roentgenological bases of hydrocephalus of the adult.) *Rev. neurol.*, May, 1950, *82*, 359–367.

This article forms part of a lengthy symposium on hydrocephalus of the adult, an official report under the directorship of Wertheimer and Dechaume. The authors discuss the anatomo-roentgenological findings of non-tumoral hydrocephalus of adults. They have combined the lumbar and ventricular methods of pneumoencephalography, thereby ascertaining the communicability of the subarachnoid and ventricular spaces. Hence the classification of non-tumoral hydrocephalus of the adult into two main types: (1) the communicating and (2) the non-communicating.

The non-communicating hydrocephalus is fully realized when the orifices leading from the subarachnoid spaces to the ventricles are impermeable. There is then a volume increase of the entire ventricular system. First, the third ventricle dilates, then the lateral ventricles and subsequently the fourth ventricle. The aqueduct of Sylvius dilates least and last. The lateral ventricles dilate most. The dilatation is considerably more than that found in tumoral hydrocephalus and is symmetrical with respect to the median-sagittal plane. However, there are mono-, bi- or tri-ventricular forms of hydrocephalus, depending on the site of the obstruction (foramen of Monro, posterior, part of third ventricle, aqueduct of Sylvius, foramen of Magendie). These obstructions may be congenital, traumatic (hematoma, edema) or inflammatory (exudative, granulomatous) in origin

The communicating hydrocephalus shows air both in the subarachnoid spaces and the ventricular cavities. Hence, external and internal hydrocephalus are generally associated. If the subarachnoid space dilatation is quite large and localized, it may displace the ventricular system, thereby rendering difficult the roentgen differentiation from tumoral hydrocephalus. In cases of cortical atrophy, there is usually an expansion of the ventricle toward the lesion.

The osseous alterations are very frequent. The cranium is ovoid, with smooth and thinned walls. The sutures are marked because of distention and recalcification. The torcular Herophili is lower. In other cases the cranium has a caved-in appearance at the anterior, middle and posterior fossae. The digital imprints are often present and are of a peculiar pattern. The diploic canals are enlarged, giving starlike porous images. The sella turcica is often depressed, decalcified and enlarged anteroposteriorly.—*J. N. Sarian, M.D.*

Vandenberg, Henry J., Jr., and Coley, Bradley L. Primary tumors of the cranial bones. *Surg., Gynec. & Obst.*, May, 1950, *90*, 602–612.

Comparatively little attention has been directed to the subject of primary neoplasms arising in the bones of the cranium, probably because of the relative rarity of such lesions. At Memorial Hospital between 1926 and 1948 the authors observed 888 primary malignant neoplasms of all bones of which only 7 (0.8 per cent) had originated in the bones of the cranium. During the same period a study of another group of 630 benign tumors of bone showed only 15 (2.4 per cent) to be of cranial origin.

The bones of the cranial vault, being ossified directly from primitive connective tissue, are not likely to develop primary tumors, while most other bones, including those of the cranial base, develop from connective tissue through a complex intermediary process of cartilage degeneration and absorption. Most primary bone tumors arise as a result of the transition incident to the development of cartilaginous or endochondral bone.

This study deals with a series of 22 neoplasms of the cranial bones of which 15 were benign and 7 malignant. Osteoma is the commonest of the benign tumors and osteogenic sarcoma is the most frequent malignant one.

Many of the benign neoplasms of the skull do not require treatment. Hemangioma may be dealt with surgically and the same may be said for some of the osteomas.

Giant cell tumor of the cranial bones is very rare. It may be treated by roentgen therapy.

Sarcoma of the skull has an extremely unfavorable outlook since, owing to its location, it does not lend itself to radical surgery. With the technical advances in neurosurgery and in view of the otherwise hopeless outlook, it is expected that there may be more radical attempts to remove the primary site of the disease in the future.

Myeloma of the skull is usually a manifestation of widespread disease. In the so-called "solitary" lesions, however, roentgen therapy may have value. —*Mary Frances Vastine, M.D.*

Grant Francis C., and Austin, George M. Epidermoids; clinical evaluation and surgical results. *J. Neurosurg.*, May, 1950, *7*, 190–198.

At present, the term "cholesteatoma" is synonymous with "pearly tumor" and "epidermoid," the latter being the term of choice. The authors have retained the name "epidermoid" as the term of preference and divided the tumors into two groups, intradural and extradural (diploic), according to their surgical location. This paper deals with the diagnosis, surgical treatment, and results of a group of 22 verified epidermoids.

Headache was the predominant symptom in 14 of these patients and apparently was not related to whether the tumor was intra- or extradural in character. Next to headache, visual disturbances were the commonest complaints, consisting of blurred vision, diplopia, or actual blindness, and were found in 8 patients. Two of these were in the extradural group. Papilledema or optic atrophy was found in 11 patients, only 1 of these being in the extradural group. In 3 patients with extradural epidermoid, the predominant complaint was a small lump on the head, and in 2 of these the lump was tender. Among the patients with intradural tumors, convulsions were noted by 4, and 3 others complained of syncopal attacks. The duration of symptoms varied from six months to eighteen years, averaging two to four years. The cerebellopontine angle has been described as the commonest site of occurrence, with the parapituitary region nearly as common.

Preoperatively, all 7 of the extradural epidermoids were diagnosed correctly by roentgenography. That these tumors give a typical roentgen picture was first pointed out by Cushing. Their sharp punched out character with frequently associated white border is almost pathognomonic. Usually the inner table is slightly more involved than the outer. Other eroding lesions, produce a defect in which the margin is less sharply defined, more hazy, and may be fuzzy and soft. One tumor, occurring in the left temporal area, was both extra- and intradural and, although classified as intradural, it showed a typical roentgen picture of erosion. The intradural group offers, a much greater challenge in diagnosis. There is usually nothing to suggest the diagnosis of epidermoid. In the series reported here, 2 of the parasellar group gave signs of sella erosion; a temporal lobe epidermoid revealed calcification; and 2 of the angle tumors showed erosion and destruction of the temporal bone. All were diagnosed preoperatively as probable tumors but not as epidermoids.

When seen at operation, these tumors are readily identified by their pearly sheen and avascular character. The only tumor presenting any similar characteristics is the dermoid. These are essentially much more cystic than the epidermoids and contain hair or other derivatives of the mesodermal corium, in addition to ectodermal structures.

Four of the 7 extradural and 4 of the 15 intradural tumors were completely removed with an over-all mortality of 22.7 per cent.—*K. K. Latteier, M.D.*

BAKAY, LOUIS. The results of 300 pituitary adenoma operations (Prof. Herbert Olivecrona's series). *J. Neurosurg.*, May, 1950, *7*, 240–255.

During the period 1929 to 1947, 292 patients with verified pituitary adenoma were treated and 300 operations performed. The series included 232 chromophobe, 55 acidophil, 2 basophil, and 3 malignant adenomas. The postoperative mortality rate was 11.3 per cent for the chromophobe and 9.5 for the acidophil adenomas. There was a striking difference, however, between the group of intrasellar tumors and the group with extrasellar extension, the first having a mortality rate of 6.4 per cent, and the second of 35.0 per cent. The estimation of the size and location of the extrasellar extension makes the operative planning easier. Encephalography, especially the filling with air of the basal cisterns, is of great help. Cases of adenomas with extension in the cavernous sinus, cave of Meckel, temporal lobe, hypothalamus, or third ventricle were included. Those in which there was extension in the cavernous sinus did not reveal a higher postoperative mortality rate than cases of the usual adenoma. There were more fatalities among patients with hypothalamic signs, and the late results of operation were not favorable.

Two years after operation or later, 54.5 per cent of the surviving patients with chromophobe adenoma were fully able to work; the ability was reduced in 27.2 per cent of the cases, and lost in 18.3 per cent. Among the acromegalic patients, the late postoperative ability to work was complete in 56.6 per cent, reduced in 23.3 per cent, and lost in 13.3 per cent (2 patients were well but did not report on ability). The radical transfrontal removal of the adenomas and the postoperative roentgen therapy in this series were followed by long survival periods and relatively few recurrences. There were 16 operations for recurrence of the adenoma. The mortality rate after secondary procedures was less than that after primary operations, and the time of survival was usually long. The late results, however, were less favorable in regard to ability to work. Recurrence rates of 10 to 15 per cent for the chromophobe and about 20 per cent for the acidophil cases are estimated. The effect of prophylactic roentgen therapy could not be analyzed on account of the lack of untreated controls, postoperative irradiation having been given in nearly all cases.—*K. K. Latteier, M.D.*

LOVE, J. GRAFTON, and MARSHALL, THOMAS M. Craniopharyngiomas (pituitary adamantinomas). *Surg., Gynec. & Obst.*, May, 1950, *90*, 591–601.

Craniopharyngiomas constitute a small but important group of intracranial neoplasms. As reported in the literature, they comprise approximately 4 per cent of all intracranial neoplasms and about 30 per cent of all pituitary tumors. They are the most frequently occurring tumors of the supratentorial cavity in children. A variety of names has been used in the literature to describe these tumors such as hypophyseal duct tumors, craniopharyngeal duct tumors, Rathke pouch tumors, craniobuccal cysts, suprasellar cysts, epitheliomas, interpedun-

cular cysts, simple squamous epitheliomas and adamantinomas.

A review of the embryologic aspects of the pituitary gland and a histopathologic study of 100 cases of so-called craniopharyngiomas demonstrates that the name "pituitary adamantinoma" is the most logical one to designate this tumor. This is true because histologically, adamantinomas are essentially epithelial growths. In reviewing the 100 cases, it was found that this tumor occurred most commonly in the second decade of life but that 47 per cent of the patients were more than 20 years old. Headache and loss of vision were by far the most common symptoms, followed by endocrine disturbances, drowsiness and signs of involvement of other neighboring structures. Roentgenologically, calcification of the tumor was observed in only 56 per cent of cases.

Ten patients experienced remission or abatement of symptoms that could be attributed definitely to roentgen irradiation.

Because it is generally felt that roentgen irradiation has little or no effect on these tumors, it might be well to give a few of the details concerning some of these patients who obtained relief. One patient who had received roentgen irradiation prior to operation was completely relieved of symptoms for a period of three years. Another patient who received preoperative irradiation experienced a remission of symptoms for two months but operation was resorted to after a second course of irradiation had failed to bring about improvement. A patient who had received a series of radium treatments followed by roentgen therapy was relatively free of symptoms for a year. Another course of roentgen radiation relieved the recurrent symptoms for four years at the end of which time he was operated upon because of bitemporal defects in the visual fields. A course of irradiation was given postoperatively, and more than a year later he was in good health and had normal visual fields and ocular fundi.

Of the 96 patients who underwent surgical operation, 38 died in the hospital, giving a hospital mortality rate of 40 per cent. At the time of this study 17 patients were known to be living a year or more after operation; of this group 13 were carrying on some type of useful activity.—*Mary Frances Vastine, M.D.*

Anzilotti, Alberto. Le leucoplasie della cavità orale. (Leucoplakia of the oral cavity.) *Radiol. med.*, May, 1950, *36*, 413–420.

The treatment of leucoplakia of the oral cavity merits further consideration because of the importance that this lesion has in the pathogenesis of carcinoma of the mouth and, above all, of the tongue and of the mucosa of the cheek.

Leucoplakia, classified by Aschoff as a chronic stomatitis, typically appears as white or grayish patches on the oral mucosa. Histopathologically they are composed of epithelial hyperplasia, hyperkeratosis and round cell infiltration. The presence of an abnormal stratum granulosum rich in keratohyaline and eleidin is characteristic.

The etiology of leucoplakia is uncertain but is probably dependent on various causes coming under two headings: general, and local.

The general causes include syphilis, tuberculosis, arthritic diathesis, chronic poisoning and avitaminosis.

The local causes include smoking, use of alcoholic beverages, improper dental fittings, poor oral hygiene. The disease is most prevalent among males fifty years of age or over.

In considering the treatment of leucoplakia, it is important to stage the disease. In stage one, the patches are circumscribed, pearly white, soft and smooth. In the second stage they may assume a villous verrucous appearance, the surface becoming roughened. The borders are more or less raised but there are no inflammatory changes.

With the appearance of inflammation, fissures, and ulcerations, the onset of malignancy is to be suspected and may be proved by biopsy.

The treatment of oral leucoplakia should be oriented in three directions: (1) having established a general cause, attempt to eliminate it if possible, or at least to modify it; (2) remove local causes to avoid recurrences; (3) treat the lesion directly according to the site and the stage of the disease.

The acceptable methods of local therapy are: (1) surgical excision; (2) diathermy coagulation; (3) radium therapy; and (4) roentgen therapy.

Surgical excision and diathermy coagulation are indicated in leucoplakia in stage one and stage two. Radium therapy and roentgen therapy are the methods of choice when there is evidence of malignancy.—*A. A. Blasi, M.D.*

Clay, Richard C., and Blalock, Alfred. Congenital arteriovenous fistulas in the mandible. *Surg., Gynec. & Obst.*, May, 1950, *90*, 543–546.

Congenital arteriovenous fistulas of bone, although uncommon, have been described but no such lesion in the mandible has been heretofore reported. The authors report 2 such cases.

In those patients in whom arteriovenous communications exist in bone, once these channels are opened by dissection, removal of the entire involved osseous segment may be the only way to control the profuse bleeding. In 1 of the cases here reported the actual arteriovenous communications were within the defect in the mandible. This patient was treated by removing the major arterial blood supply. If a progressive increase in flow through collateral channels eventually takes place, mandibular resection will be necessary to effect a cure. This is a procedure not to be undertaken lightly since it is deforming, and extensive prosthetic work will later

be required to secure good postoperative function.

Roentgenographic investigation of the mandible is advised in any case of congenital arteriovenous communication in the face or neck, whether or not pressure obliterates the thrill. If there is evidence of bone erosion, preparation for mandibular resection must be made since this may be the only way to control bleeding and to eradicate the fistulas. Such preparation should probably include dental impressions to be used if necessary in later preparation of a prosthetic device.—*Mary Frances Vastine, M.D.*

Neck and Chest

Purves, Robert K., and Wedin, Paul H. Familial incidence of cervical ribs. *J. Thoracic Surg.*, June, 1950, *19*, 952–956.

The authors state that although the occurrence of cervical rib or ribs is relatively common in that portion of the literature which they have reviewed, the familial tendency is rare.

They present a family in which the father, mother, and 5 of 10 children examined roentgenographically had cervical ribs.—*T. C. Stansbury, Jr., M.D.*

Baxter, S. G., and Munro, D. D. Benign fibroma of chest wall; report of a case. *J. Thoracic Surg.*, June, 1950, *19*, 944–951.

An unusual case of benign fibroma in that it was both intrathoracic and extrathoracic, exhibiting very rapid growth in the period of gestation, is presented.

Metastatic neoplasms of the chest wall are frequent but primary tumors of the connective tissue of the chest wall are rare. Benign tumors of the chest wall are encapsulated and lack the invasive properties of malignant lesions.

A classification of benign tumors of the thoracic wall is given. The results of surgical removal are excellent. The margin of respiratory safety in patients with large tumors exerting extrinsic pressure on the lung are extremely narrow and postoperative difficulties such as cyanosis and dyspnea occur. Early surgical extirpation is therefore recommended. —*T. C. Stansbury, Jr., M.D.*

Hendrick, James W., Ward, Grant E., and Chambers, Robert G. Carcinoma of the thyroid gland. *South. M. J.*, May, 1950, *43*, 375–384.

The authors present a good review of the literature on the subject. The early diagnosis and the necessity of a vigorous treatment are stressed.

Malignancies of the thyroid gland show great variation in their behavior and pathological manifestations, from slowly growing papillary cystadenoma to the very anaplastic, highly malignant infiltrating carcinoma.

Most investigators agree that a substantial percentage of thyroid carcinomas arise in a solitary nodule or multinodular goiter. Over 80 per cent occur in discrete adenomas or adenomatous goiters and from 7 to 20 per cent of discrete adenomas develop into malignancy irrespective of age. Carcinoma is relatively uncommon in diffuse toxic goiter; however it is frequently found in toxic nodular goiter.

The lateral aberrant thyroid tumors are discussed. The authors state that it has now been proved that these tumors represent an extension of a papillary carcinoma from the corresponding lobe of the thyroid. The primary lesion may be quite small and difficult to palpate even at operation.

Unfortunately, there are no definite signs or symptoms in the majority of cases which point to an early carcinoma of the thyroid. However, there are changes which should arouse the suspicion of malignancy. The most constant of these are the appearance of a tumor or an increase in the size of a preexisting tumor and a sense of pressure. The increase in size may be due to hemorrhage into an adenoma or to a malignant change. Occasionally the first evidence of malignancy is the development of cervical lymphadenopathy.

The authors state that if the same diligence is observed in handling thyroid nodules as in handling breast nodules better results will be achieved. They state that since 80 per cent of thyroid malignancies arise in discrete nodules surgical removal is mandatory. The accepted treatment is adequate operation and if the tumor is of high grade malignancy radiation therapy is given following surgery. Irradiation has a definite place as an adjunct to surgery. Inoperable cases are given radiation therapy only.

The role played by radioactive iodine is discussed. To be efficacious the isotope must be taken up by the tumor. It is estimated that only 15 to 20 per cent of thyroid cancers belong in this category.

The authors give a classification of thyroid carcinomas with some discussion of the pathological changes.—*J. G. Snead M.D.*

Clark, Dumont, Tempel, Carl W., and Allen, Kenneth D. A. Diagnosis of pulmonary lesions discovered by mass roentgenographic survey. *J.A.M.A.*, July 15, 1950, *143*, 943–951.

The authors point out that the small photoroentgen film used in mass roentgenography of the chest is not diagnostic but serves to indicate the presence of an abnormality which must be further identified by the usual 14 by 17 inch diagnostic film and other studies.

General diagnostic procedures are discussed. These are the routine measures ordinarily used for any diagnostic work-up, such as history, roentgen examinations, physical examination, the temperature, pulse and respiratory rates, and the blood cell count, urinalysis and sedimentation rate. Then the more specific procedures are discussed, including skin

tests for tuberculosis, coccidioidomycosis and histoplasmosis, tests for sputum and fasting gastric contents, serologic procedures, bronchoscopic examination including biopsy and cytologic examination, bronchography, and exploratory thoracotomy. Several other less commonly used procedures are mentioned briefly. It is pointed out that exploratory thoracotomy is resorted to when all the previously discussed diagnostic procedures fail to determine the nature of a pulmonary lesion. This situation most often prevails when the pulmonary lesion is a single, persistent, variable-sized, rounded density as shown in the roentgenogram. In the experience of the authors, the order of frequency of such round lesions is tuberculoma, carcinoma, and fluid-filled cyst. More rarely the following lesions occur: coccidioidomycosis, non-calcified tuberculous lymph node, lymphoma, sarcoid, neurofibroma, and hamartoma. Exploration of the thorax may be done with about the same risk as in exploration of the abdomen, due to better operative techniques, modern anesthesia, and the availability of effective antibacterial substances.

The more important diseases to be considered in the differential diagnosis of pulmonary lesions are discussed. It is pointed out that any chronic pulmonary lesion is potentially dangerous. This article is a timely discussion of the careful investigation which should be made of any pulmonary lesion found in mass surveys.—*D. S. Kellogg, M.D.*

Holman, Colin B. Roentgenology in the diagnosis of tuberculosis. *Proc. Staff Meet., Mayo Clin.*, July 19, 1950, *25*, 418–422.

The author discusses the role of roentgenology in the clinical diagnosis of tuberculosis. Through "mass survey" examinations, many lesions of the thorax were discovered. The success depended upon the accuracy of interpretation. The accuracy was influenced by (1) experience of the interpreter, (2) size, location and density of small lesions, (3) absence of roentgenologic manifestations during the latent period of three to six weeks following exposure to tuberculosis.

In many instances the interpreter is able to state whether the lesion represents tuberculosis, so that further work-up can be carried out to prove or disprove this impression. He may also give a valuable estimate regarding the probability of activity in a known tuberculous lesion—based not on a single film, but on serial studies.—*C. P. Galanti, M.D.*

Bass, H. E. Recent advances in knowledge of fungous diseases of the lungs, with special reference to coccidioidomycosis and histoplasmosis. *J.A.M.A.*, July 22, 1950, *143*, 1041–1044.

In the light of widespread endemic areas of *Coccidioides* and *Histoplasma* infections in the United States, these two fungus diseases now assume an increasing importance, particularly in the differential diagnosis of atypical pneumonias or unexplained pulmonary infiltrations.

In coccidioidomycosis an unquestionable diagnosis can be made only by isolation of the fungus. A presumptive diagnosis may be made on a negative tuberculin test or positive serologic test associated with an unchanging rounded nodule or cavity in the lung fields. The coccidioidin skin test may be of value, although cross reaction with other fungus diseases (namely histoplasmin) may occur and occasionally a negative skin test will appear in an anergic patient with coccidioidal granuloma. In regard to treatment, since the coccidioidal cavity is believed to be of a generally benign nature and since there is improbability of contagion, the conservative non-surgical approach is advocated. The treatment of disseminated coccidioidomycosis has been enhanced by the use of prodigiosin, prepared from *Bacillus prodigiosus*; further investigations are being made on the use of this material.

A presumptive diagnosis of histoplasmosis can be made in a patient with a tuberculin negative reaction and pulmonary calcification. However, pulmonary calcifications appear to be nonspecific reactions to a variety of organisms and, in particular, there may be a cross sensitivity between histoplasmosis and blastomycosis. As in the case of coccidioidomycosis, there may be anergic patients whose histoplasmin skin test is negative. Recent development of a complement fixation test for histoplasmosis will aid in more accurate diagnosis of this infection. Histoplasmin is not as yet commercially available.—*H. R. Fishback, Jr., M.D.*

White, F. Clark, and Hill, Harry E. Disseminated pulmonary calcification; a report of 114 cases with observations of an antecedent pulmonary disease in 15 individuals. *Am. Rev. Tuberc.*, July, 1950, *62*, 1–16.

During a five year period, a total of 114 patients showing disseminated pulmonary calcification were discovered in the Ray Brook State Tuberculosis District. The etiological factors which have been considered responsible for such type of calcification are tuberculosis, histoplasmosis, fungus disease, and disturbance in calcium metabolism.

All of the patients in this group were from northeastern United States. In 78 individuals a history of exposure to organic dust (dust of threshing, and that about the habitat of pigeons and domestic fowl) was elicited. Of the total group, 72 had had previous illness, and of these, 40 had had serious respiratory illness. Four familial groups were encountered, two with 2 members of the family involved, one with 3 members, and one with 4 members.

Histoplasmin and tuberculin tests were done in 84 cases, with 305 controls. The positives with both tests were much higher in the patients with calcifica-

tions than in the controls. A total of 79 cases (94 per cent) had positive histoplasmin tests and a total of 44 cases (52.4 per cent) had positive tuberculin tests.

In 15 cases there was a definite history of chronic pulmonary disease preceding the calcification. In 12 of these a detailed history was obtained, and all 12 gave a history of exposure to organic dust immediately before the initial symptoms. Films of several of these cases show a diffuse pulmonary process, followed years later by diffuse calcification. Symptoms are rare at the stage of calcification.

An autopsy was performed on one patient following accidental death. A film of the chest three weeks earlier had shown disseminated calcifications. The necropsy did not clarify the etiology of these calcifications.

It is suggested that pulmonary disease resulting in disseminated pulmonary calcifications may be an airborne infection due to *Histoplasma capsulatum* or an antigenically related fungus.—*Lois Cowan Collins, M.D.*

Kaunitz, H. Carcinoma of the lung; necessity for exploratory thoracotomy after negative bronchoscopy. *New England J. Med.*, July 13, 1950, *243*, 35–39.

Since less than 50 per cent of carcinomas of the lung have a positive bronchoscopic biopsy and since a high percentage of peripheral lesions are malignant, early exploratory procedure should be done, especially when such benign conditions as tuberculosis or lung abscess cannot be proved. The author feels that the time element is most important and that more than four weeks' delay is dangerous. Resection of an occasional tuberculous lesion is considered justifiable since it seems better to do this than to allow carcinomas to become inoperable. The only hope of cure in malignant conditions is complete excision before the tumor has spread beyond the lung.—*H. R. Fishback, Jr., M.D.*

Keil, Philip G., and Schissel, Donald J. The differential diagnosis of unresolved pneumonia and bronchiogenic carcinoma by pulmonary angiography. *J. Thoracic Surg.*, July, 1950, *20*, 62–65.

Unresolved pneumonia may simulate bronchiogenic carcinoma clinically and physically. Differentiation is often difficult and sometimes impossible even with the use of bronchoscopy, bronchography, and cytologic studies. The authors suggest pulmonary angiography as a diagnostic adjuvant. Their technique of pulmonary angiography is given.

A study of 26 patients with primary bronchiogenic carcinoma and 35 patients with resolving or unresolved pneumonia was made. Increased or normal vascularity of the involved segment was present in every case of pneumonia. Decreased vascularity within and distal to the carcinoma was present in 24 of their 26 cases. Representative roentgenograms of each group are included.—*T. C. Stansbury, Jr., M.D.*

Williams, R. B., Jr., and Daniel, Rollin A., Jr., Leiomyoma of the lung. *J. Thoracic Surg.*, May, 1950, *19*, 806–810.

The authors point out the rarity of leiomyoma of the lung in that a review of the literature revealed only 4 being reported. Of these, 2 were found at autopsy and 1 at lobectomy.

The case is reported of an eight year old white girl complaining of chronic cough of four years' duration. Chest roentgenograms had been interpreted as showing no abnormality. There were positive reactions to allergy tests and desensitization was begun. Ten months later another chest roentgenogram revealed a dense opacity measuring 10 by 7 cm. lying posteriorly over the mid-portion of the left diaphragm. Esophagus and stomach were normal on examination. Pneumonectomy was done followed by an uncomplicated course. Pathological diagnosis was leiomyoma of the lung. The patient has had no difficulty since surgery.—*R. D. Moreton, M.D.*

Daniel, Rollin A., Jr., and Williams, R. B., Jr.: Leiomyoma of the esophagus. *J. Thoracic Surg.*, May, 1950, *19*, 800–805.

The authors point out that benign neoplasms of the esophagus are very infrequently observed, and that leiomyoma is probably the most frequent among them.

Most of these tumors do not produce symptoms, and only a few have been discovered in the living. They may arise at any level of the esophagus, be solitary or multiple, but seldom are the cause of death; they may occur in any age group but are most common in elderly persons, in men predominantly.

A review of the literature revealed 92 cases of leiomyoma of the esophagus, all except 8 being found at autopsy. The 8 patients operated on for this condition are described, and 6 survived.

It is pointed out that many of these tumors can be removed without opening the esophageal mucous membrane and in such cases the mortality rate is extremely low.

The authors report the case of a thirty-eight year old white female; a growth had been found in the right chest on routine examination. There were no symptoms, but the roentgenogram of the chest revealed a well demarcated, homogeneous area of increased density measuring 6.5 by 6 cm., overlying the medial aspect of the dome of the right diaphragm. Study of the esophagus showed that it was displaced to the left but not obstructed. Exploration revealed this to be attached to the esophagus by a pedicle 3 cm. in length. Diagnosis of leiomyoma was confirmed by histopathological examination. The pa-

tient made an uneventful recovery and has remained symptom free for one and a half years.—*R. D. Moreton, M.D.*

Bruwer, Andre, Clagett, O. Theron, and McDonald, John R. Anomalous arteries to the lung associated with congenital pulmonary abnormality. *J. Thoracic Surg.*, June, 1950, *19*, 957–972.

The authors give a rather complete presentation of the embryology, pathology and clinical aspects of intralobar bronchopulmonary sequestration. Bronchopulmonary sequestration, as defined here, is limited to a lower lobe of a lung, usually the left. The lobe is found to contain a bronchiogenic cyst or cysts or a system of bronchi which does not communicate with the normal bronchial tree. This sequestrated area is supplied by a large artery which derives from the lower thoracic or upper abdominal aorta or from the celiac axis. The anomalous artery, during embryonic life caused the sequestration of the segment of pulmonary tissue in the lower lobe. Usually a large part of the lobe has never been aerated.

The authors feel that most congenital cysts of the lung may be regarded as examples of sequestration. In situations other than the lower lobes, anomalies of vascular supply are not evident but they suggest that anomalies of the intrapulmonic course of the branches of the normal pulmonary artery and vein may be the causal factors.

Any patient who presents a history of intermittent episodes of fever and cough with pain in the thorax should be suspected of having cystic disease of the lung. If roentgen examination localizes evidence of disease to a lower lobe, intralobar sequestration associated with an anomalous artery must be considered. The only adequate treatment is lobectomy.

Whenever cystic disease of a lower lobe is suspected and operation is to be performed the possibility of an anomalous artery must be borne in mind.

Five cases including reproductions of the roentgenograms and photographs of the gross specimens are presented.—*T. C. Stansbury, Jr., M.D.*

Abbott, Osler A. Experiences with the surgical resection of the human carina, tracheal wall, and contralateral bronchial wall in cases of right total pneumonectomy. *J. Thoracic Surg.*, June, 1950, *19*, 906–922.

The difficulties and lack of early diagnosis in primary bronchiogenic carcinoma are discussed. These are more marked in primary upper lobe carcinomas which tend to produce symptoms later causing confusion with pulmonary tuberculosis.

The author presents a method which is applicable to neoplastic lesions arising in the right upper lobe area and which he feels allows an extension of the indications for operability.

Experiences with the application of this procedure in 6 patients are described. Certain complications resulting from its use are discussed in detail as well as the methods used to counteract them. It is believed by the author that this method should increase the potential cure rate.—*T. C. Stansbury, Jr., M.D.*

Morton, Douglas R., Osborne, Johnston F., and Klassen, Karl P. An apparently congenital bronchoesophageal fistula persistent to adult life. *J. Thoracic Surg.*, May, 1950, *19*, 811–816.

The authors point out that the progress made in thoracic surgery, coupled with the chemotherapy and antibiotics, has accomplished the successful management of many cases of abnormal esophageal communications. Esophageal fistulas are of two main types: congenital and acquired. The latter is more frequent and may exist for a length of time without symptoms. The former manifests itself with first effort of swallowing and, if not recognized, usually results in early death of the infant.

A review of the literature is given, including the etiological factors of the acquired type. Vogt's classification of congenital esophageal anomalies is used, giving three main types: (I) complete absence of the esophagus; (II) atresia of the esophagus with an upper and lower esophageal segment, each ending in a blind pouch; and (III) atresia of the esophagus with tracheo-esophageal fistula.

The case of a twenty-six year old white male complaining of cough of several years' duration is presented. Physical finding was limited to the chest. Roentgenogram revealed increased density in the region of the right posterior basal segment, associated with a shift of the heart to the right with slight elevation of the diaphragm. A bronchogram showed severe saccular bronchiectasis of the posterior basal segment of the right lower lobe

A right lower lobectomy was done and examination of the specimen revealed a fistulous tract 2 cm. by 5 mm. in size. This was considered a congenital bronchoesophageal fistula with a right lower lobe bronchiectasis.—*R. D. Moreton, M.D.*

Nemours-Auguste. Etude de la partie terminale de l'oesophage dans le dolicho-méga-oesophage. (Study of the terminal part of the esophagus in dolicho-mega-esophagus.) *Semaine d. hôp. de Paris*, March 14, 1950, vol. 26.

It would seem that the study of dolicho-mega-esophagus (idiopathic dilatation of the esophagus, cardiospasm) has been completely exhausted but according to the author the omission has been made "to begin with the beginning." In other words, no attention has been paid to the anatomy of the

terminal part of the esophagus, its relationship to the neighboring organs and its function.

Three questions arise: (1) What is the exact anatomy of the terminal part of the esophagus in the normal and in dolicho-mega-esophagus; (2) what is its state on the operating table and at autopsy, and (3) how does it function when an alimentary bolus passes through it? These questions cannot be answered except by roentgen examination.

The region of interest extends from the so-called von Acker narrowing of the esophagus which is situated 3 or 4 cm. above the diaphragm to its entry into the stomach. This is divided into 3 parts: (a) supradiaphragmatic; (b) intradiaphragmatic, and (c) infradiaphragmatic.

(a) In the supradiaphragmatic region the esophagus is dilated during the passage of the bolus, assuming a fusiform, oval or a more or less rounded appearance, depending on age and individual variation. This portion which is of capital importance in the physiology of the esophagus is called the phrenic ampulla or the Vormagen of Luschka. Its borders are the narrowing of von Acker superiorly, the narrowing of Mouton inferiorly, and it is surrounded by pleural and vascular structures.

(b) One or 2 centimeters farther down, the esophagus enters the diaphragmatic canal where it occupies a variable position in relation to the muscle fibers forming the hiatus. Laimer's sheath which is assumed to separate the esophagus from the diaphragmatic canal was interpreted in different ways and even its existence questioned. Some authors believe that several muscle fibers connect the esophagus with the diaphragm; others are of the opinion that these muscle fibers are inserted into Laimer's sheath instead of into the esophagus, and still others consider them as simple artefacts.

(c) All authors agree that the infradiaphragmatic extension of the esophagus constitutes part of the stomach since the mucosa ends at the orifice of the hiatus.

The cardia is a zone which has no external limit and is internally demarcated by a prominence of the upper small curvature. There is no muscle of the cardia that can be demonstrated anatomically or roentgenologically.

In dolicho-mega-esophagus the von Acker narrowing is absent and there is a dilatation of the esophagus down to 1 or 2 cm. above the diaphragm. The lower portion of the greatly dilated esophagus may project on certain roentgenograms below the upper orifice of the diaphragmatic canal, creating the impression that the lesion is intra-abdominal. A more careful study, however, by changing the position of the patient and making additional roentgenograms (sometimes even in the left anterior oblique view) will show the intrathoracic localization of the distended wall of the esophagus. The filiform portion, resembling a "rat's tail," starts above the diaphragm at the level of Mouton's narrowing or epicardia, the caliber of its lumen remaining the same down to the stomach.

There are only a very few cases of dolicho-mega-esophagus reported in which autopsy findings are available. The case of Dufour is debatable, whereas Kraus found no alterations present. Likewise, the great majority of surgeons were unable to detect any organic changes at the operation, but Desplas and his followers believe that a hypertrophic stenosis of the cardia is the underlying cause of the dilatation.

The author presented elsewhere his concept of the normal anatomy and physiology of the lower extremity of the esophagus as well as his technique for the roentgen examination. It was noted that, normally, the lower extremity of the esophagus swells in a fusiform or pear-shaped manner when food accumulates. The phrenic ampulla acts as a reservoir regulating to some extent the further passage of the bolus into the stomach. It is not inconceivable, therefore, that the dilatation of the esophageal wall in dolicho-mega-esophagus is the result of a functional disorder of the phrenic ampulla, distributor of the volume of the alimentary bolus.

In summary, the author expresses the opinion that the cause of dolicho-mega-esophagus lies in the inferior part of the phrenic ampulla and not in the anatomic cardia or the diaphragmatic canal. Therefore, the words cardiospasm or phrenicospasm should be abandoned. No spasm of the inferior extremity of the esophagus exists.—*T. Leucutia, M.D.*

Whitcomb, Benjamin Bradford, and Scoville, William Beecher. Methods of marking the plane section in the open lobotomy operation. *Radiology*, May, 1950, *54*, 741–742.

Methods of visualizing the plane of section following open lobotomy are discussed. Lipiodol often enters the cerebrospinal fluid system and tantalum wire caused non-recurrent convulsions in 3 of 43 cases. Metallic tantalum powder as used by Hamby in lumbar disc surgery has been used in over 125 cases without visible harmful effects. It is simply insufflated onto the cut surface of the brain before closing.—*M. B. Goodwin, M.D.*

Fischer, F. K. Technik, Indikationen und Ergebnisse der Bronchographie mit wasserlöslichem viskösem Kontrastmittel (Joduron "B"). (Technique, indications and the results of bronchography using a water soluble, viscous contrast medium [Joduron "B"].) *Schweiz. med. Wchnschr.*, July 15, 1950, *80*, 723–734.

This article is a follow-up report on the use of a new opaque medium for bronchography. The authors use a substance called joduron "B" which is a ma-

terial of high viscosity and is water soluble. It is a preparation of an iodine salt called joduron (now commercially available—cilag) mixed with a colloidal solution of water soluble cellulose (sodium salt of glycocolic acid ether of cellulose) which is added for thickening purposes. The contrast effect of this mixture is dependent upon the joduron content (diethanolamine salt of diiodo-pyridon-N-acetic acid). The high viscosity of this mixture prevents its penetration into the alveolar substance of the lung field and this is considered its greatest asset. The authors imply that alveolar penetration is neither desirable nor advantageous. Moreover, the substance is considered less irritating to the lung tissues than other opaque substances. Animal experimentation has shown that there is very little inflammatory or other reaction in the lung.

Four hours after the instillation of the iodized mixture there is no shadow shown in the lung fields. All the contrast material has been absorbed and excreted through the urinary tract. The fate and method of elimination of the carrier fraction of the mixture is problematical. The authors feel that most of it is eliminated by coughing and expectoration, but some is eliminated by phagocytosis.

The authors have now used this contrast medium in 500 cases without harm or unpleasant reactions of any sort.

The article is well illustrated. The technique of administration is described and does not vary greatly from the American methods of gravity instillation or catheter injection. The indications for bronchography are discussed and the nomenclature of the bronchial segments as well. They use the standard nomenclature described at the London meeting of July, 1949.

They conclude that joduron "B" is equal to and better than the usual contrast media used for bronchography.—*P. C. Swenson, M.D.*

Muller, William H., Jr., and Sloan, Robert H. Experiences with the use of direct aortography in the diagnosis of coarctation of the aorta. *J. Thoracic Surg.*, July, 1950, *20*, 136–141.

Coarctation of the aorta does not usually present any diagnostic difficulties. In most instances, the site of coarctation is immediately distal to the origin of the left subclavian artery. However, it occurs occasionally in another part of the aorta or in an infantile type with several centimeters of coarctation. Contrast roentgenography gives more information about these lesions than any other diagnostic procedure.

A method of catheterization of the left radial artery and descending aorta followed by injection of 25 cc. of 70 per cent diodrast is presented. Using a small amount of opaque material a high level of concentration is placed at the point of coarctation and adequate roentgenologic contrast visualization of this defect is achieved.

The procedure has been performed on 13 patients with coarctation with adequate demonstration of the defects before operation.—*T. C. Stansbury, Jr. M.D.*

Ada, A. E. W., Jones, Oswald R., and Sheeran, Archibald D. Cholesterol pericarditis. *J. Thoracic Surg.*, July, 1950, *20*, 28–33.

Cholesterol pericarditis is an extremely rare disease. The second case of cholesterol pericarditis to appear in the English literature is reported. A brief discussion of myxedema heart and the similarities between cholesterol pericarditis and myxedema heart is presented. The etiology is obscure but the authors suggest that it could be due to degeneration of a longstanding exudate in the pericardium.—*T. C. Stansbury, Jr., M.D.*

Lindert, M. C. F., and Correll, Howard L. Rupture of pulmonary aneurysm accompanying patent ductus arteriosus; occurrence in a 67 year old woman. *J.A.M.A.*, July 8, 1950 *143*, 888–891.

This is an autopsy report of a ruptured pulmonary aneurysm associated with a patent ductus arteriosus and with the additional findings of a dissecting aneurysm of the thoracic aorta. The pulmonary aneurysm had been seen fluoroscopically ante mortem. The literature shows that over 20 per cent of the cases of aneurysm of the pulmonary artery are associated with a patent ductus arteriosus. This association should be remembered by roentgenologists.—*E. C. Baker, M.D.*

France, N. E., Levin, B., and McNicholl, B. Coarctation of the aorta (adult type) with rupture distal to the coarctation. *Arch. Dis. Childhood*, June, 1950, *25*, 175–185.

The authors point out that coarctation of the aorta is by no means an uncommon lesion. Two types are generally recognized: (1) the infantile, and (2) the adult. One of the most frequent causes of death is rupture of the aorta which is usually proximal to the coarctation.

A case is reported, of a four year old male, with no essential findings except hypertension in arms, and vigorously pulsating vessels easily palpable in supra- and infraclavicular regions. Roentgenogram of the chest showed a moderate degree of cardiac enlargement affecting mainly the left ventricle. The child ran a low-grade elevation of temperature and on the sixteenth day became acutely ill and died following a paroxysm of coughing. Postmortem examination revealed coarctation of the aorta distal to an obliterated ductus arteriosus with infective endarteritis just beyond the coarctation and rupture

forming a false aneurysm which secondarily opened into the esophagus.

Clinical reports on 13 cases of coarctation are reviewed. The coarctation was diagnosed during life in 6 cases with rupture distal to the stenosis, while in 7 cases of endarteritis without rupture a definite diagnosis was made in only 1 case, though endocarditis had been suspected in all.

Roentgen findings were reported in 10 of the 13 cases. In 4, aortic aneurysms were visualized; 2 showed opacities in the left hilar region, a widened ascending aorta was mentioned in 2 further cases and a "large aortic push" in another.

In an attempt to evaluate the part played by high blood pressure, congenital defect, and infection, a review of reported cases is given. These are discussed as to sex and age, bicuspid valves, degree of stenosis, aorta, site and character of the tear, and mycotic endarteritis.

The importance of the prevention of endarteritis, and of its early diagnosis and treatment in such cases is emphasized. It is concluded that of the three predisposing factors, mycotic endarteritis plays a much greater part in the etiology of rupture distal to the coarctation than in rupture of the ascending aorta proximal to it.—*R. D. Moreton, M.D.*

Cooley, Robert N., Sloan, Robert D., Hanlon, C. Rollins, and Bahnson, Henry T. Angiocardiography in congenital heart disease of cyanotic type. II. Observations on tricuspid stenosis or atresia with hypoplasia of the right ventricle. *Radiology*, June, 1950, *54*, 848–868.

This article is one of a series on congenital heart disease and deals entirely with tricuspid stenosis or atresia associated with hypoplasia of the right ventricle. Since the same surgical procedures of value in pulmonic stenosis are also of use in this anomaly it is important that the condition be recognized.

Tricuspid stenosis is always associated with a poorly functioning or a non-functioning right ventricle and an interauricular septal defect. Great vessel anomalies are commonly associated with this condition. The diagnosis is based on the following:

I. Patient has cyanosis.
II. Fluoroscopy shows lack of normal prominence on the right side of the heart.
III. Lack of normal prominence in the pulmonary conus region.
IV. Left axis deviation noted on the electrocardiogram.

When surgical treatment is contemplated, a more exact knowledge of the anatomy of the heart and great vessels is needed. This can be furnished by angiocardiography. The authors report 21 cases of this anomaly in which angiocardiographic findings demonstrated a malfunctioning right ventricle.

Their classification of the findings is as follows:

I. Visualization of the right ventricle.
   (a) Without transposition of the great vessels.
   (b) With transposition of the great vessels.
II. Non-visualization of the right ventricle.
   (a) Without transposition of the great vessels.
   (b) With transposition of the great vessels.

Cases are reported to illustrate each division of this classification. The main findings on the angiocardiograms are a communication between the auricles, a small or absent right ventricle shadow and a large left ventricle. The interauricular septal defect is best visualized in the anteroposterior projection, while right ventricle findings are best noted on a lateral projection. It would be advantageous to obtain simultaneous anteroposterior and lateral views so the dangers of a second injection could be avoided.

There has been about a 1 per cent mortality from the injection of the opaque medium in all the patients studied by this group.—*C. A. Stevenson, M.D.*

Evans, Elwyn. Acute nonspecific benign pericarditis. *J.A.M.A.*, July 15, 1950, *143*, 954–957.

The author reports 15 cases of acute nonspecific benign pericarditis observed in his private practice, 4 of which are reported in an addendum to the main report. He believes that this disease occurs more frequently than is generally suspected, and that in main instances it is misdiagnosed as coronary occlusion. He points out that the differential diagnosis is not difficult if one keeps the possibility in mind.

Pain was the outstanding symptom and was present in all cases. The author believes that the aggravation of the pain by respiration and body movements, such as twisting and turning, or even swallowing, is particularly important in the differentiation from coronary occlusion. Fever was present in all patients. Leukocytosis and increased sedimentation rate were present in most of the patients. Pericardial friction rub was heard in 10 of the first 11 patients. Roentgenograms of the chest showed appreciable enlargement of the cardiac shadow in 4 of the 6 hospital patients. Electrocardiographic changes indicative of pericarditis were present in 10 of the first 11 patients reported.

The association of recent or concurrent respiratory infections is noted. An acute gastrointestinal upset preceded chest pain in 2 cases.—*D. S. Kellogg, M.D.*

Gage, Mims. Acute arteriovenous aneurysm of right common carotid artery and internal jugular vein. *Ann. Surg.*, May, 1950, *131*, 617–627.

The case history of a patient with a traumatically produced arteriovenous aneurysm which ruptured after five weeks duration is described in detail. Roentgenographic interest lies in the fact that there

was no appreciable cardiac dilatation or hypertrophy although the total blood and plasma volumes were greatly increased.

The hematoma that formed following rupture of the aneurysm was the size of a grapefruit. It produced deviation, angulation and compression of the trachea, pressure on the brachial plexus, and pressure upon the carotid and return venous flow.

Four factors determine the development of cardiac dilatation after the occurrence of an arteriovenous aneurysm: (1) time (2) size of the vessels, (3) size of the opening, (4) unobstructed venous return to the heart from the arteriovenous fistula. The time factor is dependent, to a certain degree, upon the size of the vessels and the fistulous opening which determines the blood volume shunt from artery to veins to heart.

The autotransfusion of an arteriovenous fistula may be massive, moderate or minimal in volume, depending upon the size of the involved vessels, size of the opening, and distance from the heart. If the autotransfusion is massive in volume, death rapidly supervenes because of overloading of the right heart. Moderate volume of autotransfusion continued over a long period of time will result in cardiac dilatation and hypertrophy, and eventually cause cardiac decompensation if not corrected. Cardiac dilatation does not occur if the autotransfusion is of small volume.

In the present case the vessels involved were of large caliber and the opening between the artery and vein maximum, but the arteriovenous shunt did not produce cardiac effects. The internal jugular view was so compressed by the hematoma that the maximum shunt did not reach the right heart in sufficient and steady quantity to produce cardiac dilatation.—*D. R. Bernhardt. M.D.*

Gillick, Frederick G., and Schneider, Jurg. Abnormal electrokymograms from the wall of the ventricle with and without evidence of myocardial infarction. *Am. J. M. Sc.*, May, 1950, *219*, 500–512.

This report presents the electrokymographic observation of the left ventricular motion in 48 patients having in common the complaint of precordial distress; and it also presents the clinical diagnosis of a group of 18 patients who had abnormal electrokymograms of the right ventricle. The studies were taken from a series of 300 routine electrokymographic studies.

The electrokymographic and electrocardiographic tracings are presented in the cases of more than usual interest along with summaries of their histories.

Abnormal electrokymograms from the wall of the left ventricle were observed in myocardial infarction, coronary insufficiency, angina pectoris, and in patients with symptoms atypical of angina pectoris. Abnormal electrokymographic tracings can be observed in the presence of normal and borderline routine electrocardiographic studies. Fifteen of the 18 patients with abnormal electrokymograms of the right ventricle had evidence of cardiac or pulmonary disease or both.—*V. L. Peterson, M.D.*

Buyers, Robert A., and Emery, Frederic B. Pericardial celomic cysts; review of the literature and report of a case. *Arch. Surg.*, May, 1950, *60*, 1002–1005.

The author reports one case which was successfully treated by surgical removal. His patient was asymptomatic and presented a well circumscribed round mass in the anterior part of the base of the left side of the chest. The mass apparently could not be demonstrated separate from the heart. A gastrointestinal examination excluded the possibility of a diaphragmatic hernia. Inasmuch as the mass had been present for two years without change, a benign cyst was considered to be the most likely etiological possibility.

In the differential diagnosis one must consider, in addition to diaphragmatic hernia, echinococcus cysts and other parasitic cysts, eight types of congenital cysts; epidermoid, dermoid, bronchial, esophageal, gastroenteric, cystic lymphangioma and celomic cysts.

The embryonic explanation of pericardial celomic cysts is based on a study of the development of the pericardium. The pericardium originates from a series of lacunae which ultimately enlarge and coalesce to form the pericardium and its celom. The failure of these primitive lakes to merge is thought to result in the pericardial celomic cyst. Inequality in the rate of development of one of these lakes may result in the formation of a true pericardial diverticulum. Celomic pericardial cysts are usually unilocular, filled with clear or slightly sanguineous fluid and lined by a thin layer of mesothelium. They peel easily from surrounding structures.—*F. M. Windrow, M.D.*

Abdomen

Pack, George T., Moderator. The relationship of gastric ulcer to gastric cancer; panel discussion. *Cancer*, May, 1950, *3*, 515–552.

This is a record of the actual remarks of the following participants of a panel discussion: Dr. E. B. Benedict, Boston, Mass., Dr. M. W. Comfort, Rochester, Minn., Dr. R. Golden, N. Y., Dr. G. K. Higgins, N. Y., Dr. J. W. Hinton, N. Y., Dr. S. M. Jordan, Boston, Mass., Dr. J. S. LaDue, N. Y., Dr. G. McNeer, N. Y., Dr. G. T. Pack, N. Y., Dr. A. P. Stout, N. Y. and Dr. M. L. Sussman, N. Y.

Although there was considerable difference of opinion among the various participants, the subject matter was thoroughly discussed from all important aspects. It was thought that about 60 to 70 per cent of ulcers occurred in the duodenum and the remain-

ing 30 to 40 per cent were divided between benign and malignant lesions of the stomach. It was generally agreed that the average age of patients with gastric cancer was about fifty-five as compared to forty for benign gastric ulcer, but that benign gastric ulcer was about twenty times more frequent in the third decade of life than cancer, and the relative incidence of benign gastric ulcer was somewhat greater than cancer in all decades, except the eighth, in which ulcerating carcinoma was about twice as frequent as benign gastric ulcer. It was emphasized that age really gives no diagnostic assistance whatever in differentiating the lesions.

Any gastric ulcer over 2.5 cm. in diameter has 50 per cent chance of being malignant and this figure approaches 100 per cent as the ulcer increases to 4 cm. in diameter. The proportion of benign to malignant lesions in the prepyloric area and cardia of the stomach was estimated as about 50:50. On the lesser curvature of the stomach at least 75 per cent of ulcers that are difficult to distinguish from cancer are benign. On the greater curvature probably 98 per cent of ulcers are malignant. Each discussant had seen one or two benign ulcers on the greater curvature, however.

Except for the location of an ulcer on the greater curvature, its location did not influence the choice of treatment. The duration of symptoms was not thought reliable enough to influence the choice of treatment, but the longer the duration, the less the likelihood of malignancy. From 10 to 25 per cent of patients with gastric cancer give ulcer-like histories. The incidence of gastric cancer with associated benign gastric or duodenal ulcers ran as high as 30 per cent. With regard to the significance of symptoms relative to the incidence of cancer of the stomach, it was unanimously thought that even physicians with cancer of the stomach do not present themselves for diagnosis more quickly than anyone else.

Gastric ulcer was acknowledged to occur without pain in about 5 per cent of cases. Initial hemorrhage was believed to favor the presence of a benign lesion. As many as 65 per cent of patients with no free acid had cancer whereas only 2 per cent had cancer with gastric acidity of more than 60 degrees. Any symptoms referable to the stomach were thought sufficient to require roentgenologic investigation. The meniscus sign in roentgenograms of the stomach was not thought to be entirely correct in indicating the presence of a malignant ulcer. The variation in the appearance of the ulcer crater and the presence of rigidity of the gastric wall were pointed out as most reliable means of indicating a grossly malignant lesion. Roentgen studies seemed to be regarded as more reliable than gastroscopic identification, but the two methods play a complementary role.

Correct diagnosis may be made occasionally when gastric biopsy is successful. The study of exfoliative cytology of the stomach is also only occasionally reliable due to the possibility of digestion of cancer cells if gastric acidity exists. The accuracy of data obtained from the roentgenologist equals and even exceeds the diagnosis by clinical data. The importance of clinical data increases as the accuracy of roentgen diagnosis diminishes so that the diagnostic application of clinical data should have wide usefulness.

In about 10 per cent of patients in whom there was a doubt clinically as to whether the lesion might be benign or malignant it did prove to be malignant. It was also brought out that from 14 to 18 per cent of surgical specimens diagnosed macroscopically as benign ulcers were found to be cancerous on microscopic examination. Most of the discussants felt that peptic ulceration was not infrequently superimposed on cancer, but that cancer arising in a peptic ulcer was exceedingly rare. It was thought important that ulcer craters entirely disappear roentgenographically as a sign of benignancy. Failure of an ulcer to diminish in size is taken as strong evidence in favor of carcinoma. Of patients with proved gastric ulcer, about 5 per cent develop gastric cancer later on, but not necessarily at the site of the benign ulcer.

Medical treatment was recommended when the lesion appeared roentgenologically benign. The continuation of medical treatment depends upon: (1) complete disappearance of the lesion on roentgen study, including the return of flexibility of the gastric wall; (2) disappearance of blood in the stool; (3) disappearance of symptoms; (4) absolute absence of recurrence.

With the first evidence of recurrence, surgical intervention should be advised. The length of such treatment should not exceed four to eight weeks. The question of gastric resection for all gastric ulcers needs serious consideration since the cure rate in such groups is higher than for gastric cancer as a whole. The complete relief of symptoms afforded by gastric resection seemed to be almost twice as common as with medical treatment alone. It was the final opinion of the panel that there would probably be a gain rather than a loss by the routine use of gastrectomy for all gastric ulcers even though the surgical mortality rate of 5 per cent would seem to nullify the 5 per cent incidence of gastric cancer developing in patients with gastric ulcers.—*J. A. Campbell, M.D.*

Jahiel, Richard, and Feldman, Daniel J. Chronic intermittent benign dilatation of the stomach. *Am. J. Digest. Dis.*, June, 1950, *17*, 203–207.

This is a report of 2 cases in which complete retention of the gastric contents was noted for more than twenty-four hours; and in which no sign of obstruction or interference to the passage of the barium meal were found. The symptoms, during the period of retention, were minimal and exceedingly mild in nature. The roentgen picture was one of marked

dilatation and atony of the stomach associated with a patent and open pylorus, well filled duodenum and a normal jejunum. In the cases reported, retention occurred in one case during the evolution of a gastric ulcer and in the second as a complication of gastritis. Only in the second patient was surgical intervention undertaken.—*J. J. McCort, M.D.*

Palmer, Eddy D. The sarcomas of the stomach; a review with reference to gross pathology and gastroscopic manifestations. *Am. J. Digest. Dis.*, June, 1950, *17*, 186–195.

The writer has made an extensive study of the medical literature for descriptions of gastroscopically observed gastric sarcomas. He found reports of 124 cases but in less than half had there been enough information supplied to permit the reader to understand the picture which was found.

A classification of the gross forms of the gastric sacromas is given. This is as follows:

Type I. Diffusely infiltrating tumor, with an uneven or finely nodular surface but without prominent elevations, with either coarsening or obliteration of the rugal pattern.

Type II. Infiltrating tumor plaque with a few prominent projecting nodules.

Type III. Single discrete tumor, sessile or pedunculated, roughly spherical or hemispherical (as governed by its intramural relations), without peripheral infiltration.

Type IV. Ulcerated tumor with ulcer the most prominent feature, the other earlier gross characteristics having been largely destroyed thereby.

Type V. Fungating lobulated tumor, usually with multiple shallow ulcerations.

A consideration of the information presented herein reveals that the various sarcomas demonstrate no significant tendencies toward preferential sites of localization within the stomach. The preferences for gross tumor forms displayed by the different histopathologic types were no more distinctive.—*J. J. McCort, M.D.*

Clifton, Eugene E., and Young, Louis E. The serum antiproteolytic reaction of patients with lesions of the stomach and duodenum. *Cancer*, May, 1950, *3*, 488–492.

The serum antiproteolytic reactions were studied in 102 cases with proved gastroduodenal lesions. These patients were considered under seven groups: Group I, duodenal ulcers; Group II, other benign duodenal lesions; Group III, all benign gastric lesions including ulcers; Group IV, carcinoma of stomach except those with hemorrhage; Group V, all patients with hemorrhage, whatever the cause; Group VI, patients with diagnosis still in doubt, and Group VII, patients who had resections of the stomach for carcinoma, with or without clinical evidence of recurrence at the time of the test.

In Groups I, II, and III, there were 77.7 per cent negative reactions, 17.7 per cent doubtful, and 4.4 per cent positive (total of 47 cases). In Group IV, 76.5 per cent gave positive reactions, 11.7 per cent doubtful, and 11.7 per cent negative (total of 17 cases). There were only 6 patients in Group VI. Three of these patients had a preliminary diagnosis of carcinoma of the stomach and negative titer. Two had a roentgen diagnosis of carcinoma and were operated upon, but no disease was found. The other one had a cholecystectomy for chronic cholecystitis and cholelithiasis. There were 19 patients in Group VII. Twelve were examined repeatedly and found to be free of disease and gave a negative reaction. Seven patients with recurrence gave positive reaction in all but 1 instance. Elevation in titer was found to precede the clinical diagnosis of recurrence.

False positives were caused by acute hemorrhage; however, this can hardly be looked upon as a severe criticism of the test, even though it does admit the lack of specificity for carcinoma.

Out of 55 patients with negative reaction, only 3, or 5.4 per cent, had carcinoma. A negative test must not be misleading in the face of other positive findings.

False positives occurred not only in the patients with acute hemorrhage, but in patients with carcinoma who were cachectic and demonstrated widespread metastasis.

The test is suggested as a screening method which will give a high percentage of positives in gastroduodenal disease, and in the absence of acute hemorrhage compares satisfactorily with other screening mechanisms in the detection of gastric carcinoma.—*J. S. Scott, M.D.*

Weinberg, Joseph, and Greaney, E. M. Identification of regional lymph nodes by means of a vital staining dye during surgery of gastric cancer. *Surg., Gynec. & Obst.*, May, 1950, *90*, 561–567.

While there has been definite progress in the early recognition and management of gastric cancer the knowledge of the manifestations of gastric cancer has not been fully utilized as it relates to the spread of cancer by way of the lymphatics. The numerous anastomoses of the lymphatic channels in the gastric wall make it possible for cancer to spread to any part of the stomach or to any of the nodes draining the stomach. Accordingly, one should logically remove all of the stomach and all of its accessible regional lymph nodes in treating the disease surgically. Although this can be accomplished by radical total gastrectomy, the small size of the nodes and the similarity of their color and consistency to that of the tissues in which they are enmeshed (and, in many instances, the inadequacy of the exposure) makes their removal difficult or impossible.

To accomplish the more thorough eradication of the regional lymph nodes of the stomach, the authors have developed a method of staining them in vivo during surgery in order to make them more easily identified. A solution of pontamine sky blue, a bright blue staining dye, is injected into the wall of the stomach and is quickly taken up by the regional lymph nodes. This imparts to them a blue color which makes them readily identifiable. With this procedure, nodes which would ordinarily be overlooked because of their remote position or their resemblance to the surrounding tissues stand out clearly.—*Mary Frances Vastine, M.D.*

Sheehan, Vincent, and Kelly, Colm. Duodenum inversum. *Irish J. M. Sc.*, June, 1950, *6*, 288–292.

A case is reported which is of interest in three particulars: (1) The presence of a right-sided duodenum inversum which of itself had caused no symptoms. (2) Ulceration and perforation of the first portion of the duodenum. (3) Formation of a pseudopancreatic cyst, which healed after marsupialization. The authors consider that the cyst was due to the spill of duodenal contents into the lesser sac.—*J. J. McCort, M.D.*

Greenler, John J., and Curtis, Charles N. Duodenal diverticula; report of two cases. *Arch. Surg.*, May, 1950, *60*, 1011–1020.

Two unusual cases of duodenal diverticulum are reported, in both of which carcinoma of the head of the pancreas was suspected prior to surgical exploration.

In the first case, after surgical removal of a chronically infected, non-functioning gallbladder, a cholangiogram and a barium study of the duodenum both demonstrated a peculiar pocket which was thought to represent necrosis in a carcinoma of the head of the pancreas. At a second laparotomy, a duodenal diverticulum was found with the ampulla of Vater at its apex.

In the second case, inflammation of a duodenal diverticulum closed the common bile duct, producing an obstructive jaundice and leading to a preoperative diagnosis of carcinoma of the head of the pancreas.—*George Cooper, Jr., M.D.*

Golden, Ross. Some clinical problems in small intestinal physiology. Mackenzie Davidson Memorial Lecture, 1950. *Brit. J. Radiol.*, July, 1950, *23*, 390–408.

The functions of the small intestine are to secrete, absorb, and propel its contents caudad. The roentgen study of the small intestine is best carried out by fluoroscopic and film observations at intervals after administration of a meal consisting of barium in normal saline.

Movements due to the muscularis propria are of two types: peristaltic, and rhythmic, or myogenic. The first type is originated and maintained by nerve impulses; the second is not mediated by nerve impulses, and is independent of peristalsis. In addition to these, there is also independent movement of the mucosa due to the muscularis mucosae. The tonus and peristalsis of the small intestine are maintained by the parasympathetic system through the vagus, and by the sympathetic through the splanchnics. Stimulation of the vagus increases the tonus and the peristalsis; stimulation of the splanchnics decreases both if they are present, but it can also initiate movement. The stimulation of the parasympathetics releases acetylcholine at the myoneural junctions. This substance is inactivated by acetylcholine esterase which acts very rapidly. Inhibition of this esterase intensifies and prolongs the action of acetylcholine by preventing its destruction: eserine and prostigmine are such inhibitors. The chemical mediator for the sympathetics is adrenin, but its mechanism of action is not known. Two other factors are necessary for proper function of nerves in the intestine: correct concentration of potassium ions, and the presence of a certain thiamin compound.

The adequacy of the motor function of the small intestine is manifested by (1) the transit time, (2) the width of the lumen, showing the tonus, (3) the continuity of the barium shadow, (4) the speed and character of the peristaltic movements under the fluoroscope, (5) the response to the stimulus of food, and (6) the width, spacing or absence of the mucosal folds.

The average transit time is one to four hours, to the cecum. The jejunum is usually 2.5 to 3.0 cm. in width, and the ileum 2.0 to 2.5 cm. The margin should be smooth and continuous except during contractions near the head or tail of the barium column. Peristalsis is much more rapid in the jejunum than in the ileum. The mucosal folds of the jejunum are about 2 to 3 mm. in width and 2 to 4 mm. in height. They are transverse and parallel during resting, but with contraction they may become longitudinal. The ileal folds are lower, farther apart, and are often longitudinal.

Overactivity of the parasympathetics produces hypertonicity and hypermotility. This situation is seen in psychosomatic disturbances, such as anxiety states, anger, resentment, and other emotional upsets. It is also believed to play a part in recurrent, self-reducing intussusception which is occasionally seen as well as in the manifestations of food allergy in the small intestine. Parasympathetic inhibition is produced by atropine, also by a new drug, banthine, which is being used to alleviate the symptoms in ulcerative colitis, regional enteritis, and other conditions associated with parasympathetic overstimulation.

Drugs such as eserine or prostigmine, by prevent-

ing the destruction of acetylcholine, have the effect of intensifying and prolonging parasympathetic stimulation. These drugs are useful in the treatment of diseases or states associated with prolonged transit time through the smal intestine in the absence of mechanical obstruction. A special case of this type is the disease entity known as sprue, which is also marked by poor intestinal tonus and prolonged transit time. It has been found that prostigmine has little or no effect on the symptoms, but injections of mecholyl produce prompt, favorable response. Apparently this is because there is some inability of the intramural nervous apparatus to elaborate acetylcholine. Subsequent investigations have shown that the presence of abnormal fat in the small intestinal content plays a part in the abnormal motor phenomena.

Overactivity of the sympathetic division should theoretically have the same effect as parasympathetic inhibition, and this is apparently ture. Irritation of the peritoneum, which probably stimulates the sympathetics, frequently causes reflex inhibition of intestinal movements. Great abdominal pain or distress is associated with sympathetic discharge, and this may explain distention of the small intestine in these cases. Furthermore, it has been shown that epinephrine under some conditions inhibits the action of acetylcholine.

Another factor which has been recently shown to play a part is potassium. This is largely an intracellular electrolyte, whereas sodium is largely extracellular. Serum potassium may be normal in the presence of an intracellular deficit, and may be low when the ion is rapidly leaving the blood to supply the demand of the cells. Low potassium levels are associated with a mild form of paralytic ileus, apparently because potassium both plays a part in the transmission of nerve impulses and also accelerates the production or release of acetylcholine. Rapid recovery indicates that this disorder is readily reversible.

In addition to the foregoing generalized disturbances, there are three localized motor disturbances worthy of discussion. Following subtotal gastric resection there is occasionally spasm of the efferent loop of jejunum. This may be severe enough to cause obstruction, or it may be mild and asymptomatic. The basis for this temporary, frequently seen spasm has not been satisfactorily explained.

A second localized motor disturbance occurs at the site of a knuckle of bowel caused by an adhesion. The lumen of the intestine in this region is smaller than can be explained on the basis of mechanical constriction. It is apparently due to stimulation of the circular muscle directly, perhaps because of the local tension produced when the longitudinal muscles participate in peristalsis.

Localized disease of the mesentery, such as lymphangioma or carcinomatous infiltration may produce localized expansion of the adjacent segments of the small intestine. The basis for this is not known, but it may be possible that the mesenteric lesion denervates that segment of small intestine, thus making it more responsive to the normal amount of circulating epinephrine in the blood. This supersensitivity gradually disappears, and in one case observed over a period of six months, the distended loop of bowel gradually returned to normal diameter. —*E. F. Lang, M.D.*

DeBusscher, Georges. Etude radiologique du grêle au cours de diverses affections. (Roentgen study of the small intestine in various disorders.) *Acta gastro-enterol. belg.*, April, 1950, *13*, 295–350.

This is a consideration of many conditions, local and general, which may cause disturbance of the small intestine. The author states that the small intestine should be completely filled for hours after ingestion of 200 cc. of barium suspension, followed in two hours by another 200 cc. dose. The jejunum and ileum should, respectively, show uniform, continuous filling, and uniform tone, to be considered normal. The mucosal pattern of the jejunum should be regular, feathery, and may be fine or coarse; that of the ileum should be of the coiled spring variety. The only interruption allowed is that of peristaltic waves. Pyloric function and behavior of the stomach are of great importance in the type of filling of the small intestine, and irregular filling should be interpreted according to the mode of gastric emptying. The author considers a "beaded" appearance of the small intestine abnormal, but does not presume to indicate the cause. Swelling, irregularity, lack of elasticity, rigidity, and abnormalities of tonus, motility, and height of mucosal folds, are indicative of disorder in the abdomen or even of the general wellbeing and should stimulate the clinician to search for the cause.

Indications for examination are diarrhea, intestinal hemorrhage, and any abdominal pain below the level of the umbilicus.

Referring to *Nutritional disturbances* he contends that a great many conditions may cause the same roentgen picture as that frequently ascribed to B-avitamosis. Therefore, the appearance cannot be considered specific, particularly since similar irregularities may be found in the normal adult, and infant intestine. He also takes issue with the designation "disordered motor function," because it is too general, and is incomplete in that it draws attention only to the factor of motility, without taking account of tonicity, peristalsis, and degree of filling. The small intestine is an extremely sensitive organ, the roentgenological morphology of which is influenced by many factors, intra- and extra-intestinal, such as heat, cold, drugs, state of nutrition, hormonal status, state of vegetative nervous system, etc. The same individual may present differences in tone and motility on different examinations.

Neurovegetative disturbance of tone is characterized by total or segmental disturbance of the intestine, and differences in morphology may take on an anarchic form. The colon is spastic, but the time of passage through the intestine is normal.

Allergy is distinguished by great variation and irregularity in the caliber of the intestine; broad portions, with large folds, may be adjacent to hypertonic, string-like segments, and finding of such changes in the mid small intestine constitutes a very strong presumption of allergic etiology.

Chronic catarrhal enteritis is characterized by accelerated transit time, either segmental or in toto and by hypersecretion with exudate, causing flaky or granular patterns. Mucosal folds are first thickened, then may disappear with the wall becoming stiff, tubular, or uneven, in the chronic phase. The transit time of barium through the small intestine is rapid.

In the acute stage of severe *colitis*, one may find all the roentgen indications of enteritis and of neurovegetative disturbance of tone. In the course of remission phases, or in frustrated forms, the small intestine shows only slight change.

In the *fermentation syndrome* the author has seen signs of exudation (snowflake pattern) and rapid transit, particularly in the jejunum, but the sprue-like appearance is rather exceptional.

In disturbances of the *biliary tract*, there may be normal or accelerated transit time. There is rapid passage through the first loops of the jejunum, influencing unfavorably the absorption of fats. The intestine, particularly the ileum, is dystonic. Hyperperistalsis, in spite of much reduced filling, is increased, and the threshold of excitation is low. Sometimes there is gas in the jejunum, and there is almost always gas in the ileum.

In *appendicitis* the passage time is accelerated, the tone is increased throughout, or in one segment, chiefly the ileum. Peristalsis is vigorous, hypersegmentation is pronounced in the ileum, retardation and stasis may be present in the prececal part of the bowel when inflammation is present there.

In *hyperthyroidism* there is slight hypersegmentation, generalized hypertonicity, accelerated transit time, lack of tenderness on palpation of loops. The pattern is feathery and graceful. In *myxedema* the transit time is slackened by hypotonicity and hypomotility.

Helminthiasis is characterized by typical barium ingestion by worms and by pattern of barium surrounding them. Amebiasis is a disease of the large intestine and shows no characteristic findings of the small intestine.

In *Typhoid* there is irregular filling in the distal portion of the small intestine; some parts are over distended while others are not filled. There are snowflake patterns and changes such as are found in nonspecific inflammation. The passage time is normal, but some segments are stagnant while others empty rapidly. Meteorism is present at colic flexures. The lips of the ileocecal valve are thickened by hyperplasia of lymphoid tissue, presenting an appearance not unlike that seen in early, pre-ulcerous tuberculosis of the intestine.

Following *gastrectomy* the transit time is normal in 43 per cent of cases, accelerated in 28.5 per cent and retarded in 28.5 per cent. After *partial gastrectomy*, gastric emptying may be as if there were a sphincter in which case emptying of the stomach and filling of the small intestine is the same as before operation. If the stomach empties with a gush, a mass of barium collects and stagnates in the jejunum, the gastric emptying is slow and the small intestine fills rather spasmodically. The author believes that a better impression is gained if several small meals are given, rather than one large one. Long periods of diarrhea may cause a sprue-like appearance in the small intestine of the partially gastrectomized patient.

Based on the opportunity of observing one patient following total gastrectomy, he feels that there is a difference in small bowel appearance, depending upon the time following operation.

Much attention is given to *tuberculosis* and its differentiation from other terminal ileum affections. Of particular interest is the description of an early sign of ileocecal tuberculosis, which he ascribes to Marina Fiol; this is the so-called "alarm node," which is an enlargement of one or several lymphatic glands, causing a round filling defect in the margin of the presphincteric portion of the ileum. This occurs before ulceration has taken place and Fiol has followed this node through the ulcerative and cicatrization phases.

There are several conditions in the terminal ileum which must be distinguished from tuberculosis. Mild inflammation may advance to the submucosa, and to the lymph nodes, causing a follicular nonspecific ileitis. Non-sclerosing enteritis, post-typhoid ileitis, chronic bacillary dysentery, and amebiasis, must all be differentiated. He gives in tabular form a differentiation between tuberculous ileitis and regional ileitis (Crohn). Hypertrophic tuberculosis may give an appearance of tumor. Association of terminal ileitis with tuberculous ileitis is extremely rare. Simple ulcer of the ileum is likewise extremely rare; in absence of aberrant gastric or pancreatic tissue, the ulcer manifests itself by narrowing of a part of the intestine, the margins taking on an irregular design. The niche may not be recognized. In jejunal ulcer, the stenosis is more or less irregular, with stasis above the site of involvement. The niche is very difficult to demonstrate and takes the form of a round image surrounded by an inflammatory reaction zone. He concludes that there is no pathognomonic roentgenological image for tuberculosis of the small intestine and the differential diagnosis may present insurmountable difficulties.

This is an excellent review of the subject of dis-

orders, intrinsic or reflected, of the small intestine, with fifty-six illustrations, some positive, some negative, and all excellent.—*A. K. Wilson, M.D.*

WELLENS, P., and PERSYN, M. Radiologie de l'intestin grêle dans les diarrhées graisseuses idiopathiques. (Roentgenology of the small intestine in idiopathic fatty diarrheas.) *Acta gastro-enterol. belg.*, Suppl. 1, June, 1950, pp. 507–524.

This is a comprehensive article which reviews the subject adequately. Special attention is paid to the technique of examination. A tilt table with apparatus for graduated compression and rapid exposures is considered essential. The examination is made preferably after all other projected procedures since the results of the latter may orient the roentgen examination. The radiologist should be in possession of all pertinent clinical data.

In preparing the patient, all procedures which might modify the small intestinal pattern should be carefully avoided. Enemas, purgatives, painful examinations, certain drugs such as pituitrin, atropine, morphine and codeine should be prohibited. The best preparation is permitting the patient to rest. A light supper is permitted the night before. The examination may require a preliminary gastric intubation.

At the first session, a glass of barium in an isotonic suspension, is given at room temperature. The stomach is examined fluoroscopically for a gastric lesion or functional disorder. The duodenal curve is inspected to exclude stenosis in the third portion, diverticula, and evidence of pancreatic tumor.

The second session is three-quarters to one hour after the first. The important thing is to examine the patient fluoroscopically without touching him. Then the effect of simple abdominal palpation is observed; some intestines react vigorously. Observations should include the state of filling of the bowel, its appearance, motility, mobility, and sensitivity. A second glass of barium is now administered. A film is made in the position which best separates the small bowel loops as well as one in the erect position for fluid levels.

Further fluoroscopic observations and films are made at two and three hour periods. Special attention is paid to the terminal ileum. The examination is helped if the bladder is full. The patient is asked not to void after the initial observation. The Trendelenburg position and compression also may help.

The patient is then asked to eat and the ileocecal area is examined one-half hour later. The region, including the appendix, is investigated as to pain, motility, and mobility. Fims with and without compression in the Trendelenburg position are useful. A final roentgenoscopic examination is made six to eight hours after the meal and, if necessary, later. Residues in the stomach, small bowel, diverticula, and Meckel's diverticulum are sought. Ileal stasis also is observed.

Complementary examinations are passage of a Miller-Abbott tube into the small bowel; retrograde filling from a barium enema; roentgenkymography and roentgencinematography of peristalsis; effect of drugs such as atropine; investigation of other organs.

The roentgenologic anatomy and physiology are also extensively reviewed. For this purpose, the small bowel is divided into three parts. (a) The jejunum located in the left flank and periumbilical region. Here, one sees the first signs of sprue, the appearance peculiar to gastrectomy patients, multiple diverticulosis, high obstruction, ascaroides and jejunitis. (b) The end of the jejunum and most of the ileum, located about the level of the 5th lumbar and the sacroiliac joints. This is the segment which shows the changes in sprue for the longest period of time and is equally useful in the demonstration of chronic and tuberculous enteritis, ascaroides and Meckel's diverticulum. (c) The terminal ileum, located in the pelvis. This is the site of many interesting pathological processes and postoperative adhesions.

The roentgen changes due to idiopathic fatty diarrhea are described as less advanced when there is only a disordered motor function. This includes hypermotility, hypertonicity, and large irregular mucosal folds. More advanced changes are hypomotility, hypotonicity, abnormal segmentation and a scattering effect. The folds are swollen, are more separated from one another and are of variable size. The swelling may be great enough to erase the mucosal relief. There may be flocculation, dilution and fluid levels.

Hypomotility, hypotonicity, segmentation and the "scattering effect" are signs of relative atony. Edema of the intestinal wall due mainly to interference with circulation and hypoproteinemia, atrophy of the various anatomic layers and mucosal inflammation are also important factors. With progression of the disease there is regression of the roentgen pattern toward that in the newborn.

The article ends with a review of other organ changes in fatty diarrhea and a list of conditions to be considered in differential diagnosis.—*M. I. Sussman, M.D.*

HUNT, CLAUDE J. Early manifestations and radiologic indications of small bowel obstruction. *South. M. J.*, June, 1950, *43*, 469–474.

A description of simple and strangulated types of small bowel obstruction is given and the immediate and remote effects of each are discussed. In addition, the importance of the survey film of the abdomen is stressed.

There are three characteristic signs which may well be called the tripod of small bowel obstruction.

These are pain, visible peristalsis and borborygmus.

A fairly accurate differential diagnosis can be established and a decision for or against immediate operation made from a properly interpreted roentgenogram of the abdomen. In the simple type of obstruction, the blood supply to the bowel is not impaired, and thus adequate time can be taken, when indicated, for physiologic rehabilitation and bowel decompression; while in the strangulated type, gangrene and peritonitis are imminent and operation cannot be delayed.

Lockwood places great significance upon the visibility of the valvulae conniventes as a differential aid in distinguishing between simple and strangulated obstruction. It must be remembered that these markings are more apparent in the upper small bowel than in the lower and that they may still be observed early in strangulated obstruction or when the strangulation is incomplete.

The roentgen examination is the only means by which one can make an early diagnosis of small bowel obstruction and determine accurately the type of obstruction present.

When the obstructed bowel assumes the characteristic step-ladder pattern, it can be said with relative certainty that the blood supply is not in jeopardy and that adequate time can be taken to intubate the intestines, deflate them and to rehabilitate the patient physiologically.

If this pattern of bowel distention is observed, associated with an inflammatory process, it will subside as the inflammation recedes and operation for obstruction will not be necessary. In the author's experience, many of these cases subsided with the use of intestinal intubation alone.

On the contrary, if the distended loop of bowel assumes no definite pattern and is found distended in an irregular manner, is darker than in the previous type, and if the valvulae conniventes are not seen or are poorly visible, it may be said that the obstruction is one of a strangulated type; that the blood supply is impaired, and that immediate operation is imperative. Efforts toward complete physiologic rehabilitation must be deferred until after operation.

The two patterns of simple bowel obstruction and strangulation obstruction rarely occur on the same roentgenogram. If they do, the visualization of an irregular loop, dark in color and without valvulae conniventes, must be considered indicative of strangulation, and immediate operation advised.

In mesenteric thrombosis, which in reality is an obstruction since peristalsis is lacking and gangrene is imminent, the roentgenogram shows gas distributed in the small bowel.

In partial obstruction, the use of opaque medium as a diagnostic aid is stressed. Its significance centers around the rapidity of its progress through the intestinal tract. Any retardation of the barium or the detection of a malformed loop is of great significance. Frequent roentgenograms are necessary to follow the barium in its intestinal advance.

The author presents an analysis of 55 cases of his own.—*J. G. Snead, M.D.*

Heifetz, Carl J., and Senturia, H. R. Blind intestinal pouches resulting from lateral anastomoses. *Surgery*, May, 1950, *27*, 673–687.

This is a report concerning untoward features that may result from the blind intestinal pouches accompanying side-to-side anastomoses. The authors cite some of the conclusions of Cannon and Murphy who, in 1906, stated that lateral anastomosis may result in stasis which tends to enlarge the blind end of the intestine extending beyond the opening. To prevent the formation of this pouch the anastomotic opening should be made as close to the inverted end as possible. End-to-end anastomosis will avoid this hazard. References to other previously reported experimental and clinical investigations concerning this problem are included.

The 8 cases reported by the authors fall into two categories: 5 cases in which it was noted that the blind pouches produced symptoms, and 3 in which the blind pouches were asymptomatic or were coincident with other pathologic findings. A study of these cases suggests that side-to-side intestinal anastomosis, after division of the bowel, may result in a tendency for the blind end of the afferent segment to dilate. Development of a pouch may depend upon the length of the segment distal to the anastomosis, although other factors are involved such as the tonicity of the intestinal wall, the position of replaced loops at operation and stasis created by division of circular muscle fibers.

The incidence of this complication is not known. In some cases the pouches may be unrecognized at a subsequent operation because anesthesia may relax the dilated loop or it may be obscured by adhesions. The authors state that a complete review and discussion concerning recognition of these blind pouches by roentgenologic methods will be the subject of a separate communication. Reproductions of the roentgenograms in 5 cases show easily recognizable shadows of dilated pouches which contained opaque medium.

Further complications which may develop from these latent blind pouches include perforation accompanied by peritonitis, intestinal obstruction, nutritional disturbances and anemia. Perforations may result from trauma by material within the pouch. The pathogenesis of obstruction is not entirely clear, although it is suggested that the distended pouch itself exerts pressure on the efferent loop of bowel. The authors recommend a careful roentgen study of the anastomotic area of patients who have had previous abdominal operations and who complain of pain, distention, nausea, vomiting, nutritional disturbances and other symptoms of

intestinal obstruction. They conclude that blind pouches may be avoided if an end-to-end anastomosis is substituted for the side-to-side type. They state that the recognition of blind pouches is not necessarily an indication for operation. Treatment depends upon what operation has already been done, the general condition of the patient, local conditions around the pouch, the nature of the symptoms and various technical considerations.—*C. B. Holman, M.D.*

Sen, S. K. Intestinal tuberculosis. Symposium. *Indian J. Radiol.*, May, 1950, *4*, 43–53.

A general review of the diagnosis, treatment, complications, and surgical procedures used in intestinal tuberculosis is given in detail. The best form of treatment are hemicolectomy in one or two stages, and ileotransverse anastomosis, in that order. Active pulmonary lesions should be arrested before any surgical procedure is done. Primary intestinal tuberculosis is very common in India, and should always be considered in the differential diagnosis of abdominal and intestinal diseases.—*Francis O'Neill, M.D.*

Pridgen, James E., Mayo, Charles W., and Dockerty, Malcolm B. Carcinoma of the jejunum and ileum exclusive of carcinoid tumors. *Surg., Gynec. & Obst.*, May, 1950, *90*, 513–524.

Adenocarcinomas of the small intestine at the Mayo Clinic in recent years form about 1 per cent of the carcinomas of the gastrointestinal tract, including the stomach and rectum. There were 63 microscopically proved adenocarcinomas of the jejunum and ileum from 1907 through 1947 at the Mayo Clinic. Forty-four lesions were in the jejunum and 19 were in the ileum. The average age for the entire group was 49.2 years. The two sexes were affected equally in the ileac series, while men were affected about twice as often as women in the jejunal group.

The symptoms of these patients are best divided into three symptom complexes as follows: the anemic syndrome found in 68 per cent of cases, the obstructive syndrome found in 73 per cent of cases and the perforative syndrome found in 16 per cent of cases. Visible peristalsis and the palpation of an abdominal mass are the two most important signs on physical examination.

The advance of roentgenology in studying the small intestine has been dramatic in the last twenty years. In the last five years roentgen studies of the small bowel were made in 76.5 per cent of the cases and 92.3 per cent of these studies were diagnostic.

In general, the size of the tumor was proportional to the grade of malignancy, and the nodal involvement was directly related to the grade of malignancy. There were several large lesions of high grade malignancy with no nodal involvement, which lends support to the idea that tumors may be fundamentally of two types regardless of grade: those which spread by extension (the more usual route) and those which spread by vascular routes. The number and size of nodes present at operation are not a reliable index to microscopic nodal involvement. Intussusception occurred 5 times and is usually found in the presence of a polypoid type of lesion. Perforation of the bowel wall was found in a third of the cases. Neoplastic involvement of the liver occurred 6 times.

Wide resection of the lesion with removal of regional lymph nodes is the treatment of choice. A palliative short circuiting operation to divert the fecal stream around the growth is of value if resection is impossible.

In general, the higher the grade of malignancy and the greater the percentage of nodal involvement, the worse is the prognosis. The average duration of life of the patients for the entire series was 32.2 months. The prognosis in the ileac lesions was slightly better than that found in the jejunal lesions.—*Mary Frances Vastine, M.D.*

Linsman, Joseph F., and Chalek, Jack I. Hepato-diaphragmatic interposition of the small intestine. *Radiology*, May, 1950, *54*, 726–728.

Gas between the diaphragm and the liver may be due to a perforated viscus, subdiaphragmatic abscess, or intestinal hepatodiaphragmatic interposition, either by the colon or the small intestine. Interposition of the small intestine has been reported only once but the authors feel that the majority of the reported cases of colonic interposition are actually due to small intestine interposition.

Bockus states that colonic interposition may be caused by: (1) intestinal factors such as megacolon or abnormal mobility of the colon, (2) diaphragmatic factors such as muscular degeneration, phrenic nerve injury, or decreased intrathoracic pressure, and (3) hepatic factors such as ptosis, small liver, relaxation of the suspensory ligament, or fixation of the liver due to adhesions.

Colonic hepatodiaphragmatic interposition can be differentiated positively from small intestine interposition only by a barium enema. It is doubtful that either type causes any symptoms. It is important to remember that intestinal interposition and perforated viscus or subphrenic abscess can coexist at the same time.—*E. M. Cooper, M.D.*

Sloan, Wyman P., Bargen, J. Arnold, and Baggenstoss, Archie H. Symposium on some complications of chronic ulcerative colitis; local complications of chronic ulcerative colitis based on the study of 2000 cases. *Proc. Staff Meet., Mayo Clin.*, May 10, 1950, *25*, 240–244.

Sloan, Bargen and Baggenstoss found 1,104 instances of local complications in 2,000 cases of chronic ulcerative colitis. Complications, in order of frequency, were as follows:

(1) Polyposis was present in 19 per cent of the cases, or 1 in every 4 cases. Biopsy of 52 cases showed 65 per cent pseudopolyps. Fulguration of pseudopolyps apparently prevented recurrence in 71 per cent of 36 patients. Multiple polyps were far more common than diffuse polyposis.

(2) Seven per cent of the patients showed stricture formation, with the lumen narrowed to 1.5 cm. or less. The strictures were more often single than multiple, and occurred most commonly in the rectum and sigmoid.

(3) Massive hemorrhage was rare, being present in only 1 per cent of the entire group.

(4) Bowel perforation occurred in 4 per cent with the most common site being the transverse or descending colon; 28 cases developed fistula subsequent to perforation.

(5) Perirectal infection occurred in 6 per cent. Two of these patients showed secondary amyloidosis.

(6) The incidence of carcinoma could not be definitely determined; 88 cases were considered proved. The largest number of neoplastic lesions occurred in the age group between thirty and thirty-nine years. The highest carcinoma rate occurred in patients whose ulcerative colitis was present before the age of ten years. The rectum and sigmoid were the most common sites of carcinoma.—*R. C. Pendergrass, M.D.*

Jensen, Edwin J., Baggenstoss, Archie H., and Bargen, J. Arnold. Symposium on some complications of chronic ulcerative colitis; the kidney in chronic ulcerative colitis. *Proc. Staff Meet., Mayo Clin.*, May 10, 1950, *25*, 244–251.

Glomerulitis was frequently noted, but there was no evidence that chronic glomerulonephritis resulted from chronic ulcerative colitis. However, there was a direct correlation between the incidence of endothelial proliferation and the degree of activity of the colitis. Only one case of renal stone was encountered. —*R. C. Pendergrass, M.D.*

Jones, G. W., Baggenstoss, Archie H., and Bargen, J. Arnold. Symposium on some complications of chronic ulcerative colitis; the liver in chronic ulcerative colitis. *Proc. Staff Meet., Mayo Clin.*, May 10, 1950, *25*, 251–256.

Autopsy material from 91 cases of chronic ulcerative colitis was compared with that from 90 cases showing other types of enteritis or colitis, and with 57 cases in which peritonitis was present at necropsy but no evidence of enteritis or colitis. Although fatty change in the liver was common, frank cirrhosis was found in only 3 of 91 cases, an incidence no higher than that shown in routine autopsies. The authors feel that the fatty change in the liver is probably related to malnutrition and toxemia from chronic ulcerative colitis. There were 5 instances of multiple thrombi in the hepatic vessels, but only 1 case of abscess of the liver.—*R. C. Pendergrass, M.D.*

Ball, Philip, Baggenstoss, Archie H., and Bargen, J. Arnold. Symposium on some complications of chronic ulcerative colitis; the pancreas in chronic ulcerative colitis. *Proc. Staff Meet., Mayo Clin.*, May 10, 1950, *25*, 256–261.

The pancreas was studied histopathologically in 86 cases of chronic ulcerative colitis and the findings compared with those in 86 cases without colitis. The colitis group showed 46 instances of interstitial pancreatitis and there were only 3 instances in the controlled group. There were no clinical indications of pancreatic disease in the 46 cases showing histopathological changes. The authors speculated as to whether further studies might show amylase and lipase elevations. This possiblity is now being investigated. They feel that there may be some connection between the interstitial pancreatitis and the irreversibility of some cases of chronic ulcerative colitis. There was no evidence that the changes noted were the precursors of hemorrhagic pancreatitis.—*R. C. Pendergrass, M.D.*

Ritter, Joseph A., Hawthorne, Herbert R., and Metzger, Harry N. Congenital megacolon; report of three cases of the "obstructive" type treated by resection of the dilated segment in contrast to resection of the distal narrowed segment. *Pediatrics*, May, 1950, *5*, 791–798.

The authors describe the two types of megacolon: the idiopathic and the obstructive. In the former, operative procedures are not indicated, as a rule. In the obstructive type, there is an area of distal colon in which the intramural nerve plexus is lacking, resulting in physiological obstruction. Two types of surgical procedures have been devised to correct this defect. The older method consisted in resection of the dilated proximal segment of colon. More recently, Swenson has described a procedure in which the constricted segment of colon is resected and the proximal dilated segment pulled through, preserving the anal sphincter.

The authors describe 3 cases in which the older type procedure was employed by them, namely resection of the dilated proximal segment. Their results were excellent and were followed by dilatation of the constricted segment and development of propulsive movements in the formerly physiologically

inactive area. They feel that satisfactory results can be secured with either method. In none of their cases, however, does there seem to have been an adequate period elapsed postoperatively to be certain that dilatation might not recur at the resected area.—*R. M. Harvey, M.D.*

Baronofsky, I. D. Primary resection and aseptic end-to-end anastomosis for acute or subacute large bowel obstructions. *Surgery*, May, 1950, *27*, 664–672.

Five patients who had an acute or subacute obstruction of the large bowel were treated by primary resection of the segment containing the lesion, and end-to-end anastomosis. It is suggested that in certain selected cases of obstruction of the large bowel, it is possible to do primary resection and anastomosis in the presence of the obstruction, but it is not implied that this is always the procedure of choice or that it supplant other methods of treatment.

The diagnostic roentgen findings are mentioned briefly in each of the 5 cases reported. In one report it is stated that the possibility of intussusception being present was not entertained when the patient first entered the hospital, although a mass in the left upper quadrant and an absence of gas shadows in the large bowel might have suggested this possibility. It is indicated that intussusception is unusual in patients more than two years old. An analysis of 300 cases of intussusception of adults by Eliot and Corscaden showed that a tumor was found in the bowel in 40 per cent of cases; 24 per cent were benign and 16 per cent were malignant.

The author mentions that the administration of barium mixtures by mouth to patients who have an incomplete obstruction of the small bowel is likely to render such an obstruction complete. It would appear that this development might be commoner in obstruction of the large bowel because of the resorption of fluid in the colon. The author cites a report by Dennis concerning a series of 9 patients who had incomplete obstruction of the large bowel until the barium mixture was introduced by mouth or as a barium enema. After these procedures the obstructions became complete.

Subtotal colectomy, including a fairly long segment above an obstructing lesion in the descending colon, is advocated because an unsuspected lesion may be present above the site of obstruction and because of certain technical considerations. The report of Mayo and Schlicke is cited as evidence that an additional polyp or polyps are present in approximately 34 per cent of all cases in which primary cancer of the colon or rectum is found at necropsy.

The author indicates that primary resection is applicable only in selected cases.—*C. B. Holman, M.D.*

Garlock, John H., and Ginzburg, Leon. An appraisal of the operation of anterior resection for carcinoma of rectum and rectosigmoid. *Surg., Gynec. & Obst.*, May, 1950, *90*, 525–534.

In the consideration of the problem of cancer of the rectum with respect to the employment of sphincter-saving operations, the authors purposely and arbitrarily separated the organ into various levels starting 3 inches from the anal margin. For cancers below the 3 inch level, there is ample reliable statistical evidence to support the view that any operation short of the abdominoperineal resection cannot be considered radical enough to meet the requirements of good cancer surgery. This area of the rectum is intimately connected with important muscular and fascial attachments as well as contiguous viscera so that it must be considered in a different light from segments of the organ at higher levels. This distal portion of the rectum is located below the peritoneal pouch of Douglas or below the reflection of peritoneum onto the bladder in the male and the vagina in the female.

Study has shown that sphincter-saving operations should rarely, if ever, be employed for cancer of the rectum below the level of 5 inches from the anal margin because of the inability of the surgeon to excise sufficient rectum distal to the tumor to meet the requirements of radicability demanded in performance of a good cancer operation. On the other hand, this study has also shown that it is not necessary to perform an abdominoperineal resection for all cancers of the rectosigmoid and that it is possible to carry out as thorough a cancer operation with preservation of the sphincters and with a negligible incidence of local recurrence.

This paper presents the authors' experience with 163 patients who were treated for cancer of the rectum and rectosigmoid by utilizing the operation of anterior resection (saving the sphincter).—*Mary Frances Vastine, M.D.*

Marshak, Richard H. Multiple carcinomas of the large bowel. *Radiology*, May, 1950, *54*, 729–731.

Multiple simultaneous carcinomas of the large bowel are not rare and may occur in about 3.5 per cent of all cases of carcinoma of the colon.

This report is of one patient in whom four large carcinomas and one small polyp were found by roentgen methods. Surgical removal of a segment from the hepatic flexure to the sigmoid proved the presence of five separate carcinomas. Polyposis was not present.—*C. A. Stevenson, M.D.*

Levene, George, and Bragg, Ernest A., Jr. Mobility of the rectosigmoid; a new diagnostic sign. *Radiology*, May, 1950, *54*, 717–725.

The normal anatomical arrangement of the mesentery which attaches to the sigmoid and rectosigmoid portions of the colon permits motion of these two portions of the bowel. When this segment is distended with air or fluid it tends to lie close to the concavity of the sacrum while when empty it drops anteriorly and downward. Any interference with this movement may imply a disease process which fixes the bowel in one position. Examples are given where the fixation was due to pelvic adhesions, volvulus with shortening of the mesentery, pelvic tumors, metastatic malignancy in the pelvis, and primary carcinoma of the colon with extension through the bowel wall.—*C. A. Stevenson, M.D.*

O'Neill, Thomas. The dumping syndrome; an operation for its prevention. *Brit. M. J.*, July 1, 1950, *2*, 15–18.

The term "dumping" is applied to a syndrome that occurs in a high percentage of cases following gastrectomy, or less frequently, gastroenterostomy. The symptoms occur during or on completion of a meal and are characterized by weakness, nausea and a sensation of mild to severe shock. They last for about one-half hour. The condition is thought to be due to disturbance of carbohydrate metabolism and jejunal distention as a result of rapid emptying.

Based on a series of 148 cases, the author indicates that the type of operation influences the development of the syndrome. The Polya resection produced the highest percentage of cases followed by the Hoffmeister-Finsterer resection, and then the Shoemaker operation. The rapid emptying was confirmed by roentgen study in a number of cases; however, it appeared that many who were symptom-free emptied just as rapidly as those who were severe "dumpers." In others, both with and without symptoms, there seemed to be a certain amount of see-saw movement between the jejunum and the gastric remnant. The author describes his operation for a valvular anastomosis to alter the character and speed of gastrojejunal discharge.—*C. P. Galanti, M.D.*

Schottenfeld, Lewis E. Anaerobic infection of the biliary tract; a review and analysis of thirteen cases from the literature with the addition of eight new cases. *Surgery*, May, 1950, *27*, 701–719.

The author reviewed the histories of 21 patients who had an anaerobic infection of the biliary tract. The cases of 13 of these patients have previously been reported in the literature. *Clostridium welchii* was present in all but one of the cases reported. In the remaining case *Clostridium septique* was the organism present. The author mentions the four assumed possibilities of pathogenesis as being (1) descending infection from the liver, (2) ascending infection from the duodenum, (3) hematogenous infection and (4) spreading infection, usually by way of the lymphatic vessels through the wall of the gallbladder. He states that *Clostridium welchii* is found in soil, water and milk and in the intestinal canals of human beings and animals. It is a fairly strict anaerobe but is usually associated with other organisms. The bacilli alone are harmless, but they are extremely virulent when combined with even a sublethal dose of toxin. The author briefly summarizes numerous studies concerning the bacteriology of gallbladder disease and notes that there has been considerable variation in the conclusions of different investigators. The author's impression from a review of the literature is that *Clostridium welchii* is far less common and much more pathogenic than other organisms in the production of cholecystitis.

There were 11 men and 10 women in the series. The average age of the patients was 53.7 years, the oldest being seventy-two and the youngest thirty-two years of age. Thirteen patients had a previous history suggesting gallbladder disease. The presenting symptom of all patients was pain. Nine patients also had associated nausea, vomiting, abdominal distention and belching. Eleven patients showed evidence of jaundice. The patients showed no uniformity in the results of their physical examinations. Nineteen were acutely ill. A roentgenogram of the abdomen was made of each of 11 patients who were not acutely ill; 9 of the roentgenograms showed evidence of a gas-filled organ or one whose wall was infiltrated with gas. In the remaining 2 cases, the routine cholecystogram indicated an inactive, chronically diseased or obstructed gallbladder. It is suggested that many similar roentgenograms might have been obtained if the other patients had been so examined.

Laboratory determinations only suggested the presence of an acute infection in some of the 21 cases. Most of the records of operations performed indicated that an acute inflammatory process was present in the gallbladder and adjacent organs, thus emphasizing the pathogenicity of the infection. Cholelithiasis was present in 13 cases, although the character of the stone was not always described. Pus was frankly present in 7 cases. Gas, encountered in 5 cases, was noted to arise from within the wall of the gallbladder and the surrounding tissues, and was presumably generated by the organisms present. Of 16 specimens of gallbladder analyzed, gangrene and suppuration were present in 12 and acute inflammation was present in 2; in 2 there was no microscopic evidence of acute inflammation. Of the 9 cases in which roentgen study showed evidence of gas within the gallbladder, this fact was revealed by microscopic examination in only 1 instance. The presence of gas was said to have been revealed by microscopic examination in 4 of the 21 cases. The author disagrees with Lohr who contended that

leukocytes are completely absent from tissues infected with pure anaerobic cultures because in several instances in the author's series polymorphonuclear leukocytes were visible, and sometimes they were present in large numbers.

The gravity of this infection is revealed by the fact that half of all patients in this series died. Nine of 17 patients operated on died, and of 4 patients not operated on, 1 died. The author expresses the opinion that these statistics are significant in revealing whether or not operation is the treatment of choice.

He states that after a positive diagnosis, therapy should be instituted immediately and this should consist of the combined use of antibiotics, sulfonamide drugs and antigas gangrene serum. These measures should be instituted before operation is undertaken and continued until the patient is out of danger. The author emphasizes the necessity of maintaining the normal balances of water and electrolytes, as well as the use of the vitamin B complex and vitamin C for supportive therapy.

He concludes his report with detailed summaries of 8 cases which he divided into 4 groups, each of which contained 2 cases. The groups are: (1) cases without any evidence of cholelithiasis, (2) those in which stones were found only in the gallbladder, (3) those with stones in the gallbladder and common duct, and (4) those with stones in the gallbladder and common duct in which the patient had had previous operations on portions of the biliary tract.

The author emphasizes that in this type of acute cholecystitis, cholecystectomy rather than cholecystostomy is the operative procedure of choice. One roentgenogram of the abdomen which shows a gas-filled gallbladder is reproduced.—*C. B. Holman, M.D.*

Gaillard, Paul. Pancréatite aigue après cholangiographie. (Acute pancreatitis after cholangiography.) *Arch. d. mal. de l'app. digestif.*, May, 1950, *39*, 600–601.

Immediately after cholangiography, in which 15 cc. of lipiodol was injected through a colostomy tube, a patient went into very severe shock, with profuse sweating, continuous vomiting and abdominal pain. Fever developed a few hours later. The pancreatic ducts were well visualized on the roentgenograms.

The author feels that pancreatitis occurred because cholangiography was done too soon after a meal and because manometric pressure control was not used.—*Norman Simon, M.D.*

Osborne, Rollin R. Functioning acinous cell carcinoma of the pancreas accompanied with widespread focal fat necrosis. *Arch. Int. Med.*, June, 1950, *85*, 933–943.

Some malignant tumors may carry on in varying degree the functions of the tissue from which they arise. By virtue of such behavior they produce certain symptoms and signs which facilitate their recognition. It is not generally recognized that some functioning tumors of the pancreatic acini may also give rise to a peculiar clinical syndrome which is characterized by widespread focal fat necrosis. The author reports such a case and compares it with 4 other cases in the literature with almost identical clinical features. These consisted of the continuous appearance of tender nodules in the subcutaneous tissues and about the joints of the fingers and toes over a period of several months, together with intermittent fever and wasting. In all of these cases the original clinical impression was erythema nodosum. The biopsy of these nodules was reported as showing simple fat necrosis and did not give evidence of any neoplastic tissue.

The author believes that the focal areas of fat necrosis are caused by abnormally large amounts of circulating lipase and suggests that the determination of blood lipase may be an important factor in diagnosis. In support of his explanation he mentions the fact that in some instances patients with acute hemorrhagic pancreatitis have been found to have areas of focal fat necrosis in the extremities.

(This is an important contribution to the diagnosis of obscure tumors of the pancreas. It is interesting to compare this observation of focal areas of fat necrosis in carcinoma of the pancreas with the phenomenon of multiple thromboses of peripheral veins which also occurs in pancreatic neoplasm and for which no adequate explanation has been produced.)—*R. P. Barden, M.D.*

Martin, J. D., Jr., Zega, Edward L., and Adamson, N. E., Jr. Calcified cyst of the spleen; with preliminary report of experimental occlusion of the blood supply of the spleen. *Ann. Surg.*, May, 1950, *131*, 765–773.

The spleen is the least common site of occurrence of cystic disease involving the abdominal viscera. A total of 183 cases of splenic cysts are recorded in the literature, 30 of which showed calcification. An additional case of calcified splenic cyst is reported.

Splenic cysts are classified as follows: dermoid, which is extremely rare; parasitic, associated entirely with echinococcus disease; and non-parasitic which includes most splenic cysts.

The etiology of non-parasitic cysts of the spleen is unknown. Except for the neoplastic types, trauma is the only proved significant factor. There is a relative frequency of occurrence of splenic cysts in patients with antecedent splenomegaly.

Splenic cysts are usually asymptomatic. Pain due to pressure is the predominant symptom of large cysts. Associated peritoneal involvement may be manifested by severe pain, vomiting and fever. Displacement of the stomach or intestines may cause

digestive disturbances. Dyspnea and circulatory embarrassment rarely occur.

Roentgen evidence of splenic enlargement is displacement of the stomach and intestines downward and to the right. The left kidney may also be displaced downward. Pneumoperitoneum is a valuable adjunct to the roentgenographic examination.

The differential diagnosis of splenic cyst must include other causes of splenic enlargement, and cysts of the mesentery, omentum, pancreas, left kidney and left lobe of the liver. When calcification occurs in a splenic cyst, it must be differentiated from a calcified splenic or renal artery aneurysm and a calcified cyst of the liver. Splenic cysts must be considered in the differential diagnosis of any left upper quadrant mass with or without associated pain.

The treatment of cystic disease of the spleen is surgical.

Preliminary results of experimental study following occlusion of splenic blood supply in dogs are given. Infarctions and atrophy are the characteristic pathological findings. No evidence of changes suggesting cyst formation has been found up to ten weeks after operation.—*D. R. Bernhardt, M.D.*

Newman, Harry, and Pinck, Bernard D. Primary retroperitoneal tumors; a summation of thirty-three cases. *Arch. Surg.*, May, 1950, *60*, 879–896.

The retroperitoneal space lies between the peritoneum and the posterior wall of the abdominal cavity and extends from the level of the twelfth dorsal vertebra down to the base of the sacrum and the iliac crest. The lateral borders are at the outer margins of the quadratus lumborum muscles. The space is divided into the lumbar and iliac fossae.

Hansmann and Budd in 1931 advanced the theory that tumors found in the retroperitoneal space arise from remnants of the embryonal urogenital apparatus. This would explain the diversification of the pathologic types as well as the microscopic similarity with that of their respective kins of the adult urogenital tract.

The authors propose the following classification of the unattached primary neoplasms of the retroperitoneal space.

I. Cystic tumors
   (a) Dermoid
   (b) Teratoid
   (c) Developed from wolffian body
   (d) Developed from müllerian duct
   (e) Lymphatic
   (f) Traumatic
   (g) Parasitic
II. Solid tumors
   (a) Benign
      1. Lipoma
      2. Fibroma
      3. Leiomyoma
      4. Lymphangioma
   (b) Malignant
      1. Liposarcoma
      2. Myosarcoma
      3. Fibrosarcoma
      4. Neurosarcoma
      5. Lymphosarcoma
      6. Hodgkin's disease
      7. Carcinoma
      8. Undifferentiated sarcoma
   (c) Undifferentiated tumors

The retroperitoneal cysts occur more frequently in young women, being mistaken for ovarian cysts. The lipomas are likewise more common in women than men but are seen at a more advanced age; about half of them will undergo sarcomatous change. The same may be said of fibromas. Among the malignant neoplasms, lymphosarcomas and fibrosarcomas have the highest incidence. Often an exact histopathologic classification is impossible; such growths are placed in the general category of undifferentiated tumors.

The authors discuss the incidence, symptoms and diagnosis of primary retroperitoneal tumors. The differential diagnosis includes diseases of the kidney which produce a mass (hydronephrosis, polycystic disease, solitary cyst, hypernephroma, etc.) and intra-abdominal masses (hepatic tumors, splenomegaly, ovarian tumors, pancreatic cysts, tumors of the gastrointestinal tract, etc.).

The most important roentgen findings are: distortion and displacement of the bowel as demonstrated by gastrointestinal study; lateral, mesial or anterior deflection of the ureter, pressure defect of the renal pelvis and calyces, and rotation of the kidney as shown by pyelography with exposures in various positions; and obscuration of the psoas shadow with increased soft tissue density in the lumbar zone. Perirenal air insufflation is not recommended as a routine diagnostic procedure.

Windholz described an increased radiolucency of the areas involved with displacement of retroperitoneal and intra-abdominal structures as being suggestive of lipomatous tumors.

The treatment consists of total extirpation whenever possible. Roentgen therapy is recommended postoperatively in the malignant tumors and as a sole procedure in all inoperable cases.

The operative mortality is given in the literature as varying between 16 and 25 per cent and the operability rate between 7.4 and 35 per cent. Donnelly found 77 per cent of the cases to be radiosensitive.

In the authors' series of 33 cases of primary retroperitoneal tumors, 16 per cent were benign, mainly lipomas, and 84 per cent were malignant. In 53 per cent diagnosis was made by means of gastrointestinal and pyelographic studies. The tumors of 12

patients were completely extirpated. Radiation therapy was given in some of the operable and in most of the inoperable cases with definitely beneficial effects.—*T. Leucutia, M.D.*

Carter, R. Franklin, and Gillette, Lee. Immediate cholangiography; indications, technic and illustrative cases. *J.A.M.A.*, July 15, 1950, *143*, 951–954.

The authors discuss the indications and technique, with illustrative cases, of immediate cholangiography. They point out that some use this method routinely at operation, and they believe it is definitely indicated in the following situations: (1) whenever a congenital lesion of the biliary tract is suspected; (2) whenever the indications for the exploration of the common bile duct are vague or uncertain; and (3) in all secondary operations on the biliary tract for stricture of any part of the bile ducts or for suspected stones in the common duct.

The various methods of injecting the radiopaque material into the biliary tract are illustrated, such as with needles, catheters, and the T tube.—*D. S. Kellogg, M.D.*

Gynecology and Obstetrics

Mertens, Wilhelm. Lymphogranulomatose und Schwangerschaft. (Lymphogranulomatosis and pregnancy.) *München. med. Wchnschr.*, Sept. 15, 1950, *92*, 933–942.

The author relates the case histories of 4 pregnant patients who had Hodgkin's disease; he also tabulates 38 others reported in the literature. He reaches the following conclusions: If a pregnant woman has Hodgkin's disease the course of the disease is independent of the age of the patient. The incidence of lymphogranulomatosis and pregnancy is the same as in normal women. The disease occurs alike in primipara and in multipara. He could not detect any influence of the ovarian secretion on the disease. It is apparent that Hodgkin's disease does not affect pregnancy. In 64 pregnancies there occurred only 6 miscarriages. Several pregnancies occurred after the patients had developed the disease. It is very probable that Hodgkin's disease may be transmitted to the embryo via the placenta. He observed 2 children who developed the disease during the first year after birth and both mothers were suffering from lymphogranulomatosis. He estimates the probability at about 6 per cent. There also was no influence of the pregnancy on the course of the disease; interruption of the pregnancy does not improve the prognosis for the mother and is consequently not indicated. The indications for roentgen therapy in pregnant women are the same as for others provided, of course, that proper measures are taken to protect the uterus. He takes a similar standpoint regarding leukemia and pregnancy; interruption of the pregnancy is not indicated. As a matter of fact, it is his impression that the life expectancy of the mother is not worse but rather better if she is permitted to go to full term.—*E. A. Pohle, M.D.*

Bichel, Jorgen. Hodgkin's disease and pregnancy. *Acta radiol.*, May, 1950, *33*, 427–434.

Since the author has often been asked if interruption of pregnancy is indicated in women with Hodgkin's disease, he has studied 11 case histories with which he was familiar. In addition, he reviewed the literature and found detailed reports of 46 women with typical Hodgkin's disease complicated by pregnancy. Together with his 11 cases, there is a total of 57 patients. In these 57 women 65 pregnancies occurred and 42 went to term. The majority of the deliveries were normal without any obstetrical complications.

The author states that a much larger number of observations is necessary before it is possible to clarify the influence of pregnancy on Hodgkin's disease, and vice versa. However, on the basis of observations on the 57 cases, he concludes:

1. Conception frequently occurs in women suffering from Hodgkin's disease.

2. From an obstetric point of view pregnancy, parturition and the puerperium run a normal course in the great majority of cases.

3. Acute exacerbations of Hodgkin's disease are not more frequent during pregnancy than would be expected spontaneously.

4. Only 1 case is on record in which the mother died during the pregnancy.

5. Only 1 case has been reported in which it can be said, with a reasonable degree of certainty, that intrauterine transmission from mother to child took place.

6. Generally, there will be no indication for interruption of pregnancy in patients with Hodgkin's disease.—*Mary Frances Vastine, M.D.*

Portmann, U. V., and Mulvey, B. E. Hodgkin's disease and pregnancy; report of 4 cases. *Cleveland Clin. Quart.*, July, 1950, *17*, 149–153.

Four cases of pregnancy occurring in patients with Hodgkin's disease are reported. The authors state that from published reports one cannot conclude that pregnancy has any effects on the ultimate outcome. From the presented cases they call attention to the fact that pregnancy may cause an exacerbation of Hodgkin's disease. Abortion or cesarean section was not done in the authors' cases. Three of the cases were delivered normally and one died before the onset of labor.—*J. M. Dell, Jr., M.D.*

Kimbrough, Robert A., and Muckle, Craig W. Carcinoma of the endometrium. *South. M. J.*, July, 1950, *43*, 609–614.

The term endometrial carcinoma is used as it is thought to be more specific than the older terms such as carcinoma of the fundus or carcinoma of the corpus.

The article presents a good review of the subject. In addition, the results of various forms of treatment are reported in 95 consecutive cases.

Numerous etiological factors are mentioned. It has been shown that women who suffered from abnormal uterine bleeding at the menopause developed cancer three times more often than the population at large. The observation has also been made that women who had had a radiotherapeutic menopause for benign uterine bleeding were three times more often afflicted with subsequent carcinoma than would be expected. The authors quote Randall in stating that 35 per cent of women with adenocarcinoma of the endometrium had continued to menstruate beyond the age of fifty years.

Long continued administration of estrogens for relief of the subjective symptoms of the menopause undoubtedly leads to hyperplasia of the endometrium and there is increasing evidence that the development of carcinoma may be favored by this mechanism.

Postmenopausal bleeding is the outstanding symptom in the majority of cases. However, when the carcinoma occurs before the cessation of menstruation, bleeding between menstrual periods or excessive bleeding only at the time of menstruation may be the presenting symptom for many months.

Pain signifies either retention of pus or blood in the uterus or wide extension of the process to extrauterine structures. The prognosis is poor in those patients who complain of pain.

The method of treatment which gives the greatest number of five year survivals is radiation therapy (either by roentgen rays or radium) followed by surgical removal of the entire uterus and adnexa.

The authors place 100 milligrams of radium in 25 milligram units, filtered by 1 mm. of platinum in the uterine cavity and leave it in situ for forty hours, or 4,000 mg. hr. Four to six weeks later, a total hysterectomy is done. In patients who for various reasons cannot tolerate surgery, an additional radium treatment is given after a six weeks' interval. Roentgen therapy is only rarely used.

In a collected series from recent literature in which radiation therapy alone was used, the five year survival rate was 39.5 per cent, and in 1,794 collected cases of hysterectomy alone, the five year salvage was 56.8 per cent. Following what is considered ideal treatment, namely irradiation plus total hysterectomy, the five year survival rate was 70.6 per cent.

There are numerous tables. The various diagnostic procedures are also evaluated.—*J. G. Snead, M.D.*

Doyle, Joseph Bernard. Total uterine sampling; a proposed aid in the early cytologic detection of cancer. *New England J. Med.*, July 27, 1950, *243*, 121–124.

The use of a cervical spoon is described which allows for the gathering of exfoliative endometrium and scraped endocervical and stratocolumnar-junction tissue in the office. The specimens obtained after the use of this spoon are fixed in formalin and block studies are then made. The method is advocated as a screening method for detecting patients who might need further study for carcinoma for it is simple, inexpensive and not objectionable.

It is felt that this simple method, using a spoon over the cervix held in place by tampax, readily permits the establishment of indications for biopsy and further follow-up studies.—*A. J. Present, M.D.*

Taylor, Claud W. The pathology of malignant ovarian tumours. *J. Obst. & Gynaec. Brit. Emp.*, June, 1950, *57*, 328–334.

A total of 808 cases of primary ovarian neoplasm, including 171 (21.2 per cent) malignant varieties, is reported from the Women's Hospital in Birmingham. Follow-up study was possible on 161 cases of primary ovarian malignancy, 28, or 17.4 per cent, of whom were alive after five years. These were classified grossly as predominantly cystic or solid, and histopathologically as pseudomucinous, serous or anaplastic with subdivision into Grades 1, 2, or 3 malignancy, according to the cell formation. Macroscopic grading showed the cystic neoplasm to yield 28.4 per cent five year survivals and the solid 8.0 per cent. The highest salvage was from the pseudomucinous type lesions while the lowest was from those classified as anaplastic. Histopathological grading showed Grade 1 to give 65.5 per cent survival, Grade 2, 8.9 per cent and Grade 3 only 2.4 per cent.—*J. A. Martin, M.D.*

Genitourinary System

Berneike, Robert R., and Pollock, Henry M., Jr. True renal-artery aneurysm; report of a case. *New England J. Med.*, July 6, 1950, *243*, 12–14.

Aneurysm of the renal artery is an unusual lesion. Only 91 cases have been reported in the world literature. It may be "true" or "false." The "true" aneurysm comprises 85 per cent of the total number. This "true" aneurysm contains all the elements of the arterial wall and is caused by degeneration or inflammation of one or more of the arterial wall layers. Trauma is often the precipitating factor for the aneurysmal dilation of a vessel weakened by local or systemic factors.

Congenital defects of the arterial wall may be important in forming a localized weakness leading to an aneurysm. Arteriosclerosis is recognizable in only 15 per cent of the cases and syphilis in still less.

Renal artery aneurysm has been found in cases of periarteritis nodosa.

Clinically the disease occurs in both sexes, at almost any age and on either side. Pain is the most prominent symptom and is present in slightly more than half the cases. It is usually a mild, dull, aching type of pain localized in the flank or the upper abdomen. Fatal hematuria may occur if the aneurysmal sac perforates a calyx. Bleeding may result from occlusion of the renal artery, infarction of the kidney or from incomplete erosion of the renal pelvis by the aneurysm.

The tumor is recognized only when the aneurysm has reached a large size. Pulsation or a bruit may be present. Naturally, the clinical picture is influenced by the extent and direction of the hemorrhage.

Hypertension was present in 20 per cent of the cases. The blood pressure was returned to normal in 3 of 11 patients following operation.

Roentgen findings are characteristic in calcification of the aneurysmal sac. This is usually circular or wreath like and is often incomplete. The aneurysm lies anterior to the pelvis of the kidney, medial to the kidney or opposite the upper third. A large aneurysm may displace the kidney laterally and produce a pressure deformity which will be apparent first in the upper major calyx.

Treatment has been by nephrectomy including excision of the aneurysm sac. Surgery should be done as soon as the diagnosis is made since death from sudden fatal hemorrhage occurred in all reported cases in which operation was not performed. At times, the aneurysm can be excised or repaired while conserving the kidney.

The authors report a patient with a renal artery aneurysm which was observed over a two year period. During this time, the lesion increased in size 50 per cent. Symptoms were present for only two weeks prior to surgery. This feature is a helpful point in the differential diagnosis and supports the likelihood of an unfavorable prognosis in cases in which the lesion is not treated.—*F. J. Rigos, M.D.*

Armstrong, John B. A study of renal function in patients with multiple myeloma. *Am. J. M. Sc.*, May, 1950, *219*, 488–493.

The author has performed renal clearance tests in 15 patients with multiple myeloma who did not present evidence of other renal disease.

No final conclusion can be drawn from these studies as to the cause or morphological site of the renal lesion in multiple myeloma. There is no relation between the amount of proteinuria and the degree of renal damage. There was an impairment of glomerular filtration equal to or greater in extent than the tubular excretory capacity; however, the findings were not consistent.—*V. L. Peterson, M.D.*

Campbell, Meredith F. Radiologic diagnosis of urinary tract tumors in infants and children. *Radiology*, May, 1950, *54*, 646–658.

In the identification of upper urinary tract growths in the young patient, one is chiefly concerned with the mixed tumor of Wilms. Diagnosis is made with far greater accuracy by means of bilateral retrograde pyelography although excretory urography often suggests the diagnosis. For preparation, a low enema only is needed and restriction of eating is not indicated. Matthei discovered that 8 or 10 ounces of milk or formula given just before excretory pyelograms are made produces gastric distention, thus leaving a clear field through which the pelves and calyces are visualized. The author uses diodrast in doses larger than usual in performing excretory urography and makes the exposures at intervals of two or three minutes. Lower urinary tract growths are best identified by cystoscopy. Thorough cystourethroscopic study is indicated before surgical treatment is undertaken.

Renal tumors cause the following changes in pelvic outline: (1) mechanical distortion of the pelvis by the new growth, (2) obstruction of the pelvic outlet or upper ureter, and (3) ulceration due to infection and/or necrosis. Suggestive changes are elongation of the calyces, filling defect of the pelvis, and enlargement of the pelvis. Wilms' tumor must be differentiated from a renal cyst. Polycystic disease reveals a quite bizarre pelvic outline and is practically always bilateral. In the rare clear-cell renal carcinoma, usually only one calyx is involved with the appearance of the so-called "spider leg" pelvis. Epithelial tumors are also quite rare and may be expected to cause a filling defect. Adrenal tumors displace the kidney down and toward the midline. Teratomas tend to push the kidney up or down and usually outward.

Neoplasms of the bladder are visualized as irregular filling defects. They are predominantly myxomatous and grow very rapidly. The ureterocele, a congenital condition, is the most common intravesical swelling in the young. Prostatic tumors are predominantly sarcomatous, extremely rare, and rapidly fatal. They cause elongation, distortion, and irregularity of the prostatic urethra which can be demonstrated by cystourethrography. Urethral tumors are seldom seen.—*E. M. Cooper, M.D.*

Douglass, Henry L. Ureteral tumors. *Ann., Surg.*, May, 1950, *131*, 755–764.

In a series of 6,000 consecutive cases examined because of urinary symptoms, 157 patients were found to have one or more neoplasms of the urinary tract. The ureter was involved in 7 of the 157 cases of neoplasm. The case reports of these 7 patients are given in detail.

In 5 of the 7 cases the tumors were malignant. All ureteral malignancies were transitional cell

papillary carcinomas which did not readily invade normal tissue or metastasize to other structures.

Ureteral tumors were associated with gross hematuria and pain in the side and back. In no case was there a palpable mass. The preoperative diagnosis of ureteral tumor was based entirely upon urographic evidence. Direct evidence was a filling defect in the ureter at the distal end of the dilated segment. Indirect evidence of ureteral tumor was absence of a stone and dilatation of the renal pelvis and proximal segment of the ureter. Repeat urograms are useful in differentiating between tumor and blood clot. In 2 cases obvious tumors of the bladder caused concurrent tumors of the ureter to be overlooked. The majority of ureteral tumors occurred in the distal segment of the ureter.

Five patients were treated by nephro-ureterectomy. One patient was not a candidate for surgery. One patient was found to have a benign ureteral tumor after death from unrelated causes.

In cases of papillary carcinoma of the renal pelvis the corresponding ureter is predisposed to develop similar tumors. In 2 of the 5 cases of malignant tumor of the ureter the corresponding kidney had been previously removed for a similar tumor in the pelvis.

The surgical treatment of ureteral tumors is briefly discussed.—*D. R. Bernhardt, M.D.*

Œconomos, N. Dégénérescence kystique de la muqueuse des voies excrétrices ou urétérite et cystite kystique. (Cystic degeneration of the mucosa of the excretory tract or ureteritis and cystitis cystica.) *J. d'urol.*, 1950, *56*, 33–46.

This disease is characterized anatomically by cystic formations which may involve the mucosa of the pelvis, the ureter, and the bladder. Histopathologically, proliferation of the surface epithelium is found followed by cystic degeneration. Clinically, most cases present as an infection syndrome. The disease has no relation to polycystic disease of the kidney. The pathogenesis is unknown, but most cases occur in adults with a past history of urinary infection with or without pain. They are seen most often either with a renal colic or hematuria. This history, associated with pyuria, is most commonly the reason for consulting a physician.

On urography, dilatation of the urinary tract is found. There may be ureteral strictures but the outstanding finding is the scalloped outline of the pelvis and ureter, so that they may look worm-eaten.

Cystoscopically, small cysts are seen most often around the ureteral orifice. The appearance simulates bullous edema. The cysts may look clear, grayish, or hemorrhagic.

In the differential diagnosis, there must be considered tuberculosis, polycystic disease of the kidney, diffuse papillomatosis, non-opaque calculi, chronic pyelonephritis, and bullae (air).

The disease is chronic and progresses slowly. The prognosis is good providing the complications of infection and hematuria do not become serious.—*M. L. Sussman, M.D.*

Miller, Hazen L. Multiple malignancy; report of a case with synchronicity in kidney and bladder. *Urol. & Cutan. Rev.*, July, 1950, *54*, 401–404.

The author presents a case of synchronous malignancy in the urinary system. The patient whose record is included in this report had a primary papilloma of the urinary bladder and a hypernephroma involving the upper pole of the right kidney.

This article emphasizes the importance of careful evaluation of the upper urinary tract in patients with neoplasms of the urinary bladder.—*G. W. Chamberlin, M.D.*

Nervous System

Wood, Ernest H., Jr., and Himadi, George M. Chordomas: a roentgenologic study of sixteen cases previously unreported. *Radiology*, May, 1950, *54*, 706–716.

Chordomas arise from remnants of the notochord and are of relatively low malignancy. They occur twice as frequently in men as in women and are rarely found in children. Grossly, these neoplasms are rounded or lobulated masses of soft, gelatinous tissue with areas of hemorrhage, necrosis, and calcification. Fragments of cartilage and bone are found where the tumor has invaded the bone. For some unknown reason metastasis occurs only from these tumors which arise in the sacrococcygeal area and are usually to the regional lymph nodes; however, blood-borne metastases to the viscera have been reported.

In the 16 patients with pathologically verified chordomas, these tumors were found in the following locations: in the clivus in 7 patients, in the nasopharynx in 1, in the vertebrae in 5, and in the sacrococcygeal regions in 3.

Chordomas of the clivus usually cause destruction of the sphenoid sinuses, nasopharynx, and occasionally the ethmoids. Calcified particles are frequently seen. Ventriculography will usually show upward displacement of the third ventricle and posterior displacement of the fourth ventricle and cerebral aqueduct.

Vertebral and sacrococcygeal chordomas produce osteolysis of two or more vertebrae and invade the intervertebral discs. Myelography may show an epidural mass compressing the dural sac. Whenever a mixed osteoclastic and osteoblastic reaction is

observed one must consider the diagnosis of chordoma.

At the present, treatment consists of conservative surgical excision and external irradiation but only a small percentage of patients will show a favorable response. The ultimate prognosis for patients with chordoma is poor.—*E. M. Cooper, M.D.*

Neuhauser, E. B. D., Wittenborg, Martin H., and Dehlinger, Klaus. Diastematomyelia; transfixation of the cord or cauda equina with congenital anomalies of the spine. *Radiology*, May, 1950, *54*, 659–664.

Diastematomyelia is a congenital malformation of the neural axis and spinal cord with a sagittal division of a segment of the cord. The cord or cauda is transfixed by an osseous or fibrocartilaginous septum.

The authors believe the diagnosis can be made in most cases by roentgenograms. There is a widening of the neural canal and the interpedicular spaces which may extend over three to six adjacent spinal segments. The involved pedicles are not narrowed. A definite diagnosis is then established by the visualization of a midline bony or fibrocartilaginous spicule 1.0 or 1.5 cm. in length. If this is not calcified and therefore not seen on the anteroposterior roentgenogram, it should be demonstrable on the myelogram. There are commonly other associated anomalies of the spine.

Treatment consists of operative removal of the midline septum. A detailed report is to be published.—*E. E. Seedorf, M.D.*

Skeletal System

Christie, Amos, Martin, Margaret, Williams, Edwin L., Hudson, Granville, and Lanier, James C., Jr. The estimation of fetal maturity by roentgen studies of osseous development. *Am. J. Obst. & Gynec.*, July, 1950, *60*, 133–139.

This is a preliminary report of studies made to determine the accuracy of estimating fetal maturity from osseous development seen on the roentgenograms of fetuses in utero. For the fetal studies, anteroposterior and right anterior oblique, and occasionally left anterior oblique and lateral roentgenograms were obtained. The presence or absence of the distal femoral epiphysis and the proximal tibial epiphysis, the estimated weight of the fetus and the estimated length of gestation in weeks were recorded from 100 such roentgenograms.

The weight of the fetus estimated from the films differed from the birth-weight estimate by less than 500 grams in 76 per cent and by less than 750 grams in 92 per cent of the cases studied.

The authors conclude that: (1) the average weight of the fetus increases with the number of centers of ossification present; (2) the determination of maturity solely from the presence of the centers for the distal femur and proximal tibia would result in appreciable error in about 10 per cent of the cases when both centers were either present or absent and in about 20 per cent of the cases when only the distal femoral epiphysis was present.—*Gerald Lavner, M.D.*

Trevor, David. Tarso-epiphysial aclasis; a congenital error of epiphysial development. *J. Bone & Joint Surg.*, May, 1950, *32-B*, 204–213.

Tarso-epiphysial aclasis is a congenital growth disorder of the tarsus and of the epiphyses. The paper is a clinical and roentgenological study with, in some cases, a report of the operative findings in 8 patients. The site generally involved was the knee or ankle joint, both knee and ankle together in 5 patients, the knee joint alone in 2 and the ankle joint alone in one.

The changes in the roentgenogram are confined to the epiphyses, the metaphysis being normal. In the case of the knee joint, there is enlargement of the femoral epiphysis, and sometimes of the tibial epiphysis. The enlargement grows from the epiphysis back towards the popliteal space above the epiphysial line, extending also inward on the medial side and outward on the lateral side. The appearances suggest a mass of cartilage tissue in which there are several foci of ossification. In older children the separate foci have fused, thus giving rise to a more uniform appearance throughout the growth. The changes are seen in only half of the epiphysis.

When the medial side of the ankle was affected, the medial malleolus was enlarged, and on the medial side of the talus there was a surface growth extending medially, irregular and enlarged—sometimes twice the size of that on the opposite side and as big as the calcaneum. When the navicular and the cuneiforms were affected, singly or together, the ossific nucleus appeared early; instead of one center there were several small foci. When the lesion occurred in the lateral side of the ankle the roentgen changes were similar.

Tarso-epiphysial aclasis is clinically distinct from dyschondroplasia and from diaphysial aclasis and no confusion should arise. In dyschondroplasia and in diaphysial aclasis the essential changes are found in the metaphysis. Dysplasia epiphysialis punctata, although easily distinguished clinically, may be confused with tarso-epiphysial aclasis roentgenographically. In dysplasia epiphysialis punctata, particularly when the tarsus is involved, the stippling effect occurs in the epiphysis and extends throughout its whole width. The shafts of the long bones may be thickened and shortened and the metaphysis splayed. In tarso-epiphysial aclasis, the stippling effect arises from the epiphysis, and in case of the epiphyses of the long bones, from one-half only, and the metaphysis appears normal.

The condition is considered to be a congenital error of development of the skeleton. It is suggested that the etiological factor affects the limb buds during early fetal life. The arrangement of the blood vessels explains, possibly, why the condition is confined to one-half of the epiphysis. It may explain also the several foci of ossification that occur in the cartilaginous mass as it grows from the epiphysis. Failure of the peripheral cells of the epiphysis to degenerate in the normal way causes a mass of cartilage to grow from the peripheral surface and accounts for the generalized enlargement of a bone such as the talus. The failure to confine these peripheral cartilaginous cells, derived from the mitotic annulus, suggests the term tarso-epiphysial aclasis for this affection.

If the projecting mass can be removed without causing instability of the affected joint, it should be removed. But when the outgrowth is extensive its complete excision may necessitate stabilization of the joint. Trevor states that this should be undertaken only if it is fully justified by the severity of the disability, and it is seldom necessary.

In the series of cases, there was no instance of the inner side of the knee joint being involved with the outer side of the ankle, or vice versa. When there was change in both knee and ankle joints, the inner side of the knee with the inner side of the ankle, or the outer side of the knee and the outer side of the ankle, was the rule.—*R. S. Bromer, M.D.*

Milman, D. H., and Bakwin, H. Ossification of the metacarpal and metatarsal centers as a measure of maturation. *J. Pediat.*, May, 1950, *36*, 617–620.

This article discusses the use of centers of ossification of the epiphyses of certain metacarpal and metatarsal bones as measures of bone maturation in the age group between one and five years. They find the most useful bones to be the epiphyses for the first and second metacarpal bones and the second, third, and fourth metatarsal bones. The authors employ the tables obtained by Francis and Werle from a study of approximately 300 boys and 300 girls in Cleveland on whom a series of 1,728 observations were made over a five year period. From their data the authors constructed curves plotting age against ossification percentages. They have also constructed age ranges for the appearance times of the various epiphyses of the metatarsal and metacarpal bones which would form a good quick reference for those concerned with bone maturation problems. Separate charts are illustrated for the hand and foot of both boys and girls.—*R. M. Harvey, M.D.*

Chiari, H. Ueber multiple Exostosenbildung an der Wirbelsäule bei Akromegalie. (The formation of multiple exostoses about the vertebrae in acromegaly.) *Wien. klin. Wchnschr.*, July 7, 1950, *62*, 473–476.

After a detailed study of the spine of an acromegalic, Chiari describes the formation of rather marked, sharp, jagged and scalloped exostoses about the processes and ligamentous insertions of the vertebrae, and minimizes the occurrence of marginal new bone about the surfaces of the vertebral bodies which was previously considered to be characteristic of acromegaly by Erdheim. These changes are chiefly in the lower thoracic and upper lumbar regions and involve the articular, transverse and spinous processes, decreasing the usually visualized normal spinal curves and occasionally compromising foramina. These exostoses are ascribed to the response of bone to ligamentous strain in the presence of abnormal bone growth in acromegaly. Chiari reports these findings in a convincing manner with an exhaustive description of the material studied.—*L. A. Nash, M.D.*

Claireaux, Albert E., and Lewis, Ian C. Reticuloendothelial granuloma: a review with a report of a case of Letterer-Siwe disease. *Arch. Dis. Childhood*, June, 1950, *25*, 142–150.

The authors, reporting from the University of Edinburgh, discuss the reticuloendothelial granulomas, pointing out the similar clinical features of the various disorders produced.

Eosinophilic granuloma of bone produces multiple skeletal lesions, with little evidence of systemic upset and with recovery as the usual outcome, unless there is a severe intercurrent infection. The pathologic picture is one of eosinophils in a granulomatous lesion composed of solid masses of histiocytes. The lesions may regress spontaneously or may be effectively treated by roentgen therapy with or without curettage.

Hand-Christian-Schüller disease may have other symptoms than the classic triad (exophthalmos, diabetes insipidus, and multiple lesions of the skull), depending on the site of the pathologic process. The pathologic picture in this entity is of masses of histiocytes dominated by foam cells. The mortality is 30 per cent but the prognosis is better for older children and adults in whom the disease is more chronic. Treatment is supportive, by special diet, and by roentgen therapy (it is important to note that the exophthalmos is refractory to roentgen treatment).

Letterer-Siwe disease usually appears before the age of two years, runs an acute course, and is fatal in a few weeks or months. Siwe described the following diagnostic signs: (1) marked splenomegaly with moderate to pronounced hepatomegaly; (2) a hemorrhagic tendency, chiefly manifested by petechiae or purpura; (3) generalized enlargement of lymph

nodes which are discrete and not tender; (4) localized defects in bones which may be detected only by roentgen examination or at necropsy; (5) the blood picture is that of a progressive non-regenerative anemia; (6) the disease is neither hereditary nor familial, and occurs exclusively in infants; the onset is acute and the outlook is unfavorable; the duration varies from weeks to months; the etiology is unknown; (7) the characteristic lesions show a pathologic picture of generalized hyperplasia of histiocytes in various organs, especially the spleen, liver, lymph nodes, thymus, skin, and bone marrow. The authors' case presented these features.—*S. H. Fisher, M.D.*

Fairbank, H. A. Thomas. Paget's disease. *J. Bone & Joint Surg.*, May, 1950, *32-B*, 253–265.

In this article the author gives a description of Paget's disease. After defining the condition as one of slowly spreading changes in one or more bones, consisting of decalcification coupled with hyperostosis and with the marrow spaces in the bone occupied, partially or completely, by vascular fibrous tissue, he describes the hereditary and familial influences, the age and sex incidence and the skeletal distribution. In regard to the etiology, the cause is unknown. The signs and symptoms are discussed in detail and, following this, the roentgenographic appearances. The changes in the bone are divided into four types: (1) honeycombed or spongy; (2) striated; (3) dense; and grossly (4) cystic. Mention is made of Thurstan Holland who called attention to the appearance of striation in the calcaneum while the bone was still apparently unaffected by the disease, which Holland regarded as an early sign of some diagnostic value. Though there may be a preference in some cases for one particular type of change, Fairbank states that there is general agreement that in most cases there is a tendency for affected bones to become denser in the course of time.

Complications of the disease are discussed, with mention of fractures, the incidence of complicating sarcoma and with mention of 3 cases in which a malignant osteoclastoma developed as reported by Russell. Multiple myeloma, co-existing with Paget's disease, has also been reported. Following the section on complications, the pathology and differential diagnosis are considered. Leontiasis ossea can be excluded if there is localization of the thickening to only one part of the calvarium, by absence of the gross type of mottling with woolly circular spots of dense bone and by obvious involvement of the facial bones, at least on one side of the face. Secondary carcinomatosis from the breast or stomach and particularly from the prostate in the male, has to be excluded. Other conditions to be excluded are fluorosis, dense vertebrae in Hodgkin's disease, hyperparathyroidism and, in exceptional cases, chronic infection.

Roentgenograms of 11 cases are reproduced. This article is an excellent and concise description of the disease.—*R. S. Bromer, M.D.*

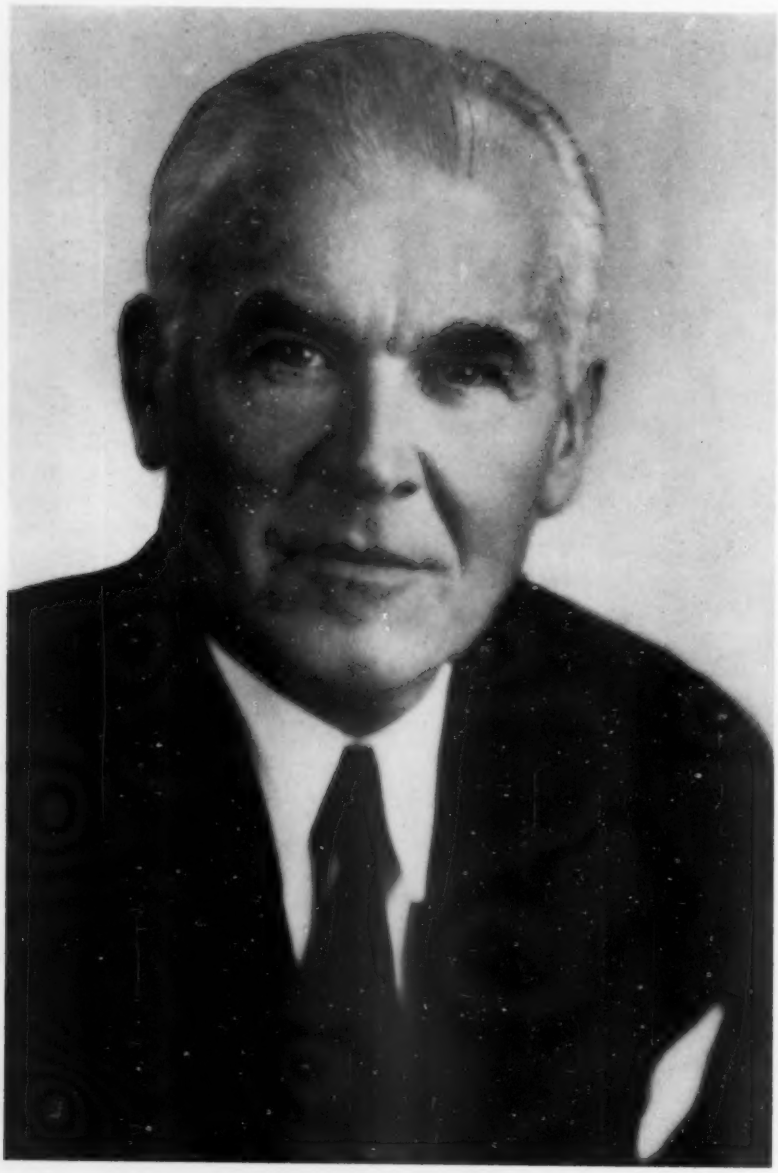
Fairbank, H. A. Thomas. Neurofibromatosis. *J. Bone & Joint Surg.*, May, 1950, *32-B*, 266–270.

This article on the skeletal changes in neurofibromatosis follows the pattern of Fairbank's previous contributions on the various skeletal diseases. After defining the disease, sections follow on the hereditary and familial influences, age and sex incidence, etiology, clinical signs, roentgenological appearances, progress, complications, pathology and diagnosis.

The skeletal affections are of two kinds—scoliosis and changes in the bones. The latter are said to occur in 7 per cent of the cases and are usually free from symptoms. Skin and bone lesions may be superimposed. They may be associated with diminution or accentuation of growth of a bone, the latter being more common and rarely seen without soft tissue changes in the neighborhood. The various roentgenological appearances are fully described.

In the section on pathology, Fairbank states that he has discovered no clear statement as to the nature of the pathological changes in a bone showing diffuse density with neither cyst formation nor erosion of the cortex by a subperiosteal neurofibroma. Tanner considered that sclerosis was a late development following earlier rarefaction and softening. Collagenous and myxomatous degeneration in osseous lesions, with formation of cysts containing brownish fluid, the result of hemorrhage, were mentioned by Thannhauser. Fairbank believes that the neurogenic origin of those bone lesions which are subperiosteal is readily acceptable, but this is not so with those that are endosteal. However, the typical fibrosis with "whorls" of cells has been found in some lesions apparently endosteal. The cause of the scoliosis where there is no cystic or other lesion in a vertebral body is obscure. It has been suggested that the deformity is due to derangement of tonic nervous control of the vertebral muscles.

Three roentgenograms of one patient are included. This article as the others previously contributed by the author is a concise and excellent description of the disease with an ample bibliography.—*R. S. Bromer, M.D.*



H. L. BOCKUS

CALDWELL LECTURER, 1950